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MAGNITUDE OF MALARIA, ASSOCIATED FACTORS, AND ITS EFFECTS ON COAGULATION AND HEMATOLOGICAL PROFILES AMONG ADULT PATIENTS AT WOLKITE UNIVERSITY SPECIALIZED TEACHING HOSPITAL, CENTRAL ETHIOPIA: A CROSS-SECTIONAL STUDY

MSC THESIS

BY

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Magnitude of Malaria, Associated Factors, and Its Effects on Coagulation and Hematological Profiles among Adult Patients at Wolkite University Specialized Teaching Hospital, Central Ethiopia: A Cross-Sectional Study

A Thesis Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements for Master of Sciences in Medical Parasitology, Medical Laboratory Sciences.

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LIST OF ABBREVIATIONS

APTT	Activated Partial Thromboplastic Time
CHMI	Control Human Malaria Infection
K3 EDTA	Potassium Ethylene Diamine Tetra Acetic Acid
INR	International Normalization Ratio
IPD	Inpatient Department
ISI	International Sensitivity Index
ITN	Insecticide-Treated Net
MC	Malaria Complicated
MM	Mild Malaria
MN	Malaria Negative
MP	Malaria Positive
MPV	Mean Platelet Volume
MU	Malaria Uncomplicated
OPD	Outpatient Department
PT	Prothrombin Time
ROC	Receiver Operating Characteristic
SM	Severe Malaria
WKUSTH	Wolkite University Specialized Teaching Hospital

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ABSTRACT

Background: Malaria remains a significant global health issue, affecting hematological and coagulation profiles. Though there have been many studies on the magnitude of malaria and its associated factors worldwide, studies are limited in this study area.

Objective: To assess the prevalence of malaria associated factors, and its effects on coagulation and hematological profiles among adult patients at Wolkite University Specialized Teaching Hospital from February to April 2024.

Methods: A cross-sectional study involving 286 malaria suspected patients was conducted using a consecutive sampling technique. Data on sociodemographic, clinical history were collected using a structured questionnaire. Coagulation profile analysis using Urit 610 coagulometer, hematology profile analysis using a Zybio Z30 hematology analyzer, and blood film microscopy. Data was entered into EpiData 3.1 and transferred to SPSS version 26 for analysis. Binary logistic regression, the Mann-Whitney U test, and receiver operating characteristic were employed to analyze the data. Statistical significance was set at a p-value of less than or equal to 0.05.

Results: The prevalence of malaria was 41 (14.3%). Risk factors included a history of malaria (AOR = 3.724, 95% CI: 1.316-10.537), stagnant water near homes (AOR = 4.118, 95% CI: 1.801-9.413), and nighttime outdoor exposure (AOR = 4.505, 95% CI: 1.677-12.106). Travel history (AOR = 3.365, 95% CI: 1.238-9.146) increased infection risk, while insecticide-treated net use was significantly protective (AOR = 6.208, 95% CI: 2.380-16.191). Malaria-infected patients exhibited prolonged prothrombin time and activated partial thromboplastic time compared to non-infected. White blood cell counts, neutrophils, and monocytes were elevated. Red blood cells, and hemoglobin, platelets were decreased. The best diagnostic values for malaria were monocyte count, red cell distribution width, and platelet distribution width.

Conclusions: Community awareness is necessary to promote regular screening for individuals with a history of malaria, eliminate stagnant water near homes, encourage the use of insecticide-treated nets, and highlight the risks of nighttime outdoor exposure. Healthcare providers should closely monitor the impact of malaria on coagulation and hematological profiles to optimize diagnostic strategies and predict disease severity.

Keywords: Malaria, associated factors, coagulation and hematological profiles.

1. INTRODUCTION

1.1 Background

Malaria is a devastating infectious disease caused by protozoan parasites of the genus *Plasmodium*(1).Five species are known to infect humans: *plasmodium falciparum (P. falciparum), plasmodium vivax (P. vivax), plasmodium knowlesi (P. knowlesi), plasmodium ovale (P. ovale*), and *plasmodium malariae (P. malariae)* (2).

The risk factors for malaria infection include not using insecticide-treated nets (ITNs), presence of stagnant water, overnight stays in rural areas, proximity to streamlets, lack of malaria transmission information, low income, lack of malaria prophylaxis, and open eaves in houses (3,4).

The life cycle of Plasmodium comprises two hosts, humans and Anopheles mosquitoes; the cycle commences after an infected mosquito injects sporozoites into the human bloodstream through a blood meal (5).These sporozoites move to the liver, attach to hepatocytes, and reproduce, producing merozoites that enter the bloodstream. Merozoites then invade red blood cells, undergo asexual reproduction, and eventually burst, releasing more merozoites to continue the cycle (6). Some parasites develop into gametocytes, which are swallowed by mosquitoes during subsequent blood meals, then in the mosquito, gametocytes mature and can infect new humans, perpetuating the cycle (7).

The pathogenesis of malaria involves complex interactions between parasite biology and host immune responses (8). Immunopathological changes and dysregulation of cytokine production play central roles in disease severity, with endothelial barrier disruption during parasite sequestration contributing to organ damage (9). Clinical manifestations can affect multiple organs, including the liver, kidneys, and eyes, with potential long-term consequences (10).

Microscopic examination of Giemsa-stained thick and thin blood films continues to be the gold standard for malaria finding, allowing species determination based on morphological characteristics (11). Rapid diagnostic tests (RDTs) serve as useful supplements, offering quick and easy-to-use alternatives, especially in resource-limited settings (12).

Molecular techniques like polymerase chain reaction (PCR) provide higher sensitivity and assist in definitive species identification, though their use is limited due to high costs and specialized requirements (11).

Malaria can be prevented and controlled through two main strategies: vector control, which involves using insecticide-treated bed nets, indoor residual spraying (13), and larvicide to reduce mosquito populations; and chemoprophylaxis, where antimalarial medications are taken before, during, and after travel to malaria-endemic regions to prevent infection (14).

Endothelial damage and the release of pro-inflammatory cytokines disrupt normal clotting and leads to bleeding due to depletion of clotting factors in malaria patients often reveal abnormalities such as prolonged prothrombin time (PT), activated partial thromboplastic time (APTT), and an elevated international normalized ratio (INR) (15). These findings suggest that malaria can cause clotting dysfunctions, with such abnormalities being particularly pronounced in *P. falciparum* infections. In fact, prolonged PT and APTT are more common in these cases, and they are found to correlate with the levels of parasitemia(16). Additionally, malaria can cause coagulation disorders such as disseminated intravascular coagulation (DIC), where excessive clotting in small blood vessels leads to bleeding due to the consumption of clotting factors (17).

Hematological profiles in malaria-infected patients show elevated white blood cell (WBC) counts, neutrophils, and monocytes, whereas hemoglobin (HGB) and platelet (PLT) counts may also be reduced, and red blood cell (RBC) indices can show variations (18).Anemia, especially in *P. falciparum* infections, is a common finding (17). The destruction of RBCs by plasmodiumparasites leads to anemia; increased PLT consumption due to immune responses contributes to thrombocytopenia, while leukopenia may result from suppression of WBC production (19). Thrombocytopenia, often observed in both *P. vivax* and *P. falciparum* malaria, is typically associated with parasitemia levels (20).

The underlying mechanisms of these hematological and coagulation disturbances by malaria parasites are complex. Parasite-induced endothelial damage disrupts normal clotting, and the release of pro-inflammatory cytokines further contributes to coagulation abnormalities, including DIC (19,21).

1.2 Statement of the Problem

Globally, malaria continues to be a major global health challengethere were an estimated 263 million cases and 597 000 malaria deaths occurring annually(22).Respiratory problems, impaired consciousness, convulsions, prostration, hypotension/shock, jaundice, severe anemia, bleeding/DIC, hyper parasitemia, and hypoglycemia are among the serious side effects of this mosquito-borne illness, which are commonly linked to coagulopathy and micro vascular abnormalities(23).

In Africa, the burden of malaria is particularly severe; the continent accounts for 92% of global malaria cases, and nearly 80% of malaria-related deaths occur in 17 African countries. Of these, 53% of deaths are concentrated in just 7 countries, highlighting the high stakes of malaria management in the region (24–27). Sub-Saharan Africa bears the brunt of the continent's malaria burden, with the disease being one of the top three causes of communicable disease deaths in the region. The high prevalence and mortality rates underscore the critical need for effective malaria control and treatment strategies (24–27).

Ethiopia faces a substantial malaria burden as well, with approximately 75% of the country’s land area being endemic. This exposes over 68 million people (about 75% of the population) to malaria. The country reports 4-5 million malaria cases annually and approximately 70,000 malaria-related deaths each year. *P. falciparum* and *P. vivax* are the predominant species, responsible for 69% and 31% of cases, respectively. Malaria significantly affects social and economic development, accounting for 30% of the overall disease burden (24, 27, 28).

In Wolkite Town, malaria is still a major health concern. From 2015 to 2018, the Wolkite health center's malaria prevalence trend was 8.56%, with *P. vivax*being the most common species(29).

Significant variations in PLT, PT, and APTT between malaria patients and healthy controls suggest that both intrinsic and extrinsic coagulation pathways are activated (30). The most significant predictors of malaria infection are low PLT, WBC, and lymphocyte counts, which are all significantly altered by malaria infection(18).

The study showed that patients with a high probability of receiving a negative malaria blood film result can be identified using a platelet count of ≥185,000 cells/µl as a screening criterion (31). Platelet indices like MPV, PDW, PCT (plateletcrit), and immature platelet fraction (IPF %) can predict malaria severity. Elevated MPV and PDW, decreased PCT and platelet count, and increased IPF% indicate severe malaria (32).

The study found that malaria is substantially linked to thrombocytopenia, neutropenia, low MCV, low MCH, low MCHC, high RDW, and microcytic hypochromic anemia (33). Another study also found that low hemoglobin, white blood cell, and platelet counts are associated with malaria infection, especially in adults with mild parasitemia. These hematological changes could potentially be used as indicators of malaria risk in endemic areas (34).

Despite these findings, there is a notable gap in data regarding the magnitude of malaria and its associated factors in relation to coagulation and hematological profiles among adults in this area. Specifically, there is limited data on the current magnitude of malaria infections and their relationship with coagulation profiles and the diagnostic value of selected hematologic profiles for predicting malaria severity.

This study aimed to fill this gap by investigating local data from Wolkite catchment areas between February and April 2024. The objectives were to identify the magnitude of malaria infections, analyze associated factors, and explore their effects on coagulation and hematological profiles.

1.3 Objectives of the Study

1.3.1 General Objective

- To assess the prevalence of malaria, associated factors, and its effects on coagulation and hematological profiles among adult patients at Wolkite University Specialized Teaching Hospital (WKUSTH) from February to April 2024.

1.3.2 Specific Objectives

- To assess the prevalence of malaria among adult patients at Wolkite University Specialized Teaching Hospital from February to April 2024.
- To identify the associated risk factors of malaria among adult patients at Wolkite University Specialized Teaching Hospital from February to April 2024.
- To determine the effects of malaria on coagulation profile among adult patients at Wolkite University Specialized Teaching Hospital from February to April 2024.
- To determine the diagnostic value of selected hematological profiles in predicting the severity of malaria among adult patients at Wolkite University Specialized Teaching Hospital from February to April 2024.

1.4 Research Question/Hypothesis

1. What is the magnitude of malaria in the study population?
2. What are the factors associated with malaria in the study population?
3. Does malaria have an effect on the coagulation profile in the study population?
4. Do selective hematologic profiles have significant diagnostic value to predict the severity of malaria?

1.5 Significance of the Study

Malaria remains a leading cause of morbidity and mortality in many parts of sub-Saharan Africa, including Ethiopia. This study provided important information on the magnitude of malaria, its associated risk factors, and its effects on coagulation and hematological profiles among adult patients at WKUSTH.

This study provided the key data on the current malaria prevalence in WKUSTH and identifies risk factors associated with malaria. It was helped to make informed decisions on where to focus resources, improve malaria prevention programs, and develop better strategies to reduce the disease's impact.

This study was also help to understand how malaria affects coagulation and hematologic profiles. It identified the key diagnostic value of selected hematologic profiles for predicting malaria. This helped with the clinician’s ability to diagnose and manage malaria-related issues, leading to better patient care.

This finding provided information identifying the key risk factors of malaria, helping the community raise awareness of health education on how to take preventive measures.

Furthermore, it could provide baseline data for others interested in the field to conduct additional research.

1.7 Operational Definition of Variables

Prothrombin Time (PT) test: is an extrinsic clotting system and screening test. The reference range of PT is approximately 11-15 seconds (35).

Activated partial thromboplastic time (APTT) test: the time in seconds required for a fibrin clot, which measures the intrinsic and common coagulation pathways. The reference range of APTT is approximately 24-35 seconds (35).

Mild malaria: malaria parasite density < 1000 parasites/μL of blood.

Moderate malaria: malaria parasite density from 1,000 to 9,999 parasites/μL of blood.

Severe malaria (≥10,000 parasites/μL of blood) (34,36).

Uncomplicated Malaria: This includes mild to moderate malaria.

Complicated Malaria: This involves severe malaria (36).

Anemia is defined as Hemoglobin less than 13 g/dL for adult males and less than 12 g/dL for non-pregnant women (37). Wolkite's elevation ranges from 1910 to 1935 meters above sea level; the recommended adjustment would be 1.1 g/dl. An individual's measured hemoglobin level is taken at this altitude; this was reduced by 1.1 g/dl to assess anemia according to WHO guideline sea-level standards (38).

Thrombocytopenia is caused by a platelet count of less than 150 x 109/L and can be classified as mild (PLT, 100–150 x 109/L), moderate (PLT, 50–100 x 109/L), or severe (PLT, <50 x 109/L) (37).

Leukopenia: defined as a total white cell count (WBC) of less than 4×109/L(37).

2. LITERATURE REVIEW

2.1. Prevalence of Malaria

In 2022, an estimated 249 million cases of malaria and 608,000 malaria-related fatalities occurred worldwide in 85 countries; 95% of malaria fatalities (580,000) and 94% of cases (233 million) occurred in the African area(39). A cross-sectional study conducted in Sabah, Malaysia, revealed that the magnitude of malaria infection was approximately 33.6%, indicating that about one-third of the community had malaria(40).

In Nigeria, a cross-sectional and descriptive study revealed an overall magnitude of malaria parasite infection of 65.6% among the study population (41). A cross-sectional study in three pastoral communities in the Western-North region of Ghana obtained a malaria magnitude of 39.1%. The magnitude was significantly advanced among ladies (23.0%) and children under 5 years (12.6%). High points of home possession (83.9%) and the use of ITNs (96.2%) were observed in the town (42).In Bossaso, Somalia, a community-based, systematic cross-sectional study reported a malaria magnitude of 19.7%, indicating malaria as a significant public health concern among adults in the area and indicating numerous contributing factors (43).

A systematic review and meta-analysis conducted in Ethiopia created a pooled frequency of malaria among adults of 13.61%. Subgroup analysis revealed that the magnitude among characteristic and symptomless grown-ups was 15.34% and 11.99%, correspondingly. Regional analysis indicated that the maximum magnitude was in the Southern Nations, Nationalities, and Peoples' Region (SNNPR) at 16.17%, followed by Oromia Regional State (13.11%) and Amhara Regional State (12.41%) (44).In the Dembiya District of the North Gondar administrative zone in the Amhara Regional State, a study revealed the total magnitude of malaria parasites to be 22.4%, with *P.falciparum* being the predominant species (45).

Facility-based cross-sectional studies in Wogera District, Ethiopia, originated that out of 585 children who provided blood samples, 51 (8.7%) were diagnosed with malaria. The principal Plasmodium species were *P. falciparum* (65%) and *P. vivax* (35%) (46).An institutional-based cross-sectional study in named health centers around Lake Tana, Ethiopia, reported that of 531 febrile patients, 75.3% were malaria negative and 24.7% had verified malaria cases (47).

A community-based cross-sectional study in Mizan-Aman Town, Ethiopia, originated an overall malaria magnitude of 21.1%, with *P. falciparum* accounting for the majority of cases (48). A retrospective study conducted at Wolkite Health Center in the Gurage Zone of Ethiopia reported that, out of 121,230 clinically suspected malaria cases, 8.56% were microscopically verified(29).

2.2. Associated Risk Factors of Malaria

A study in Burkina Faso discovered that rainfall and temperature were completely and significantly associated with malaria frequency, with a pause time of 9 and 14 weeks, respectively. Spatial analysis revealed that malaria cases were more likely to happen near each other, with persistent hotspots recognized. Additionally, low socioeconomic status was powerfully associated with malaria hotspots (49). A cross-sectional study conducted in Sabah, Malaysia, revealed that males and individuals living in rural areas were at significantly increased risk of malaria infection. The study concludes that malaria is predominant in Sabah and is powerfully associated with specific socio-demographic and geographical factors (40).

A systematic review and meta-analysis to characterize the literature and assess the strength of associations observed that bed net possession was statistically associated with a reduced threat of malaria, controlling for environmental things. Bed net use and distribution were observed to have a significant defensive effect, while the impact of other factors, such as disease control programs, was a smaller amount clear (50).

A cross-sectional study conducted in Lake Tana, Ethiopia, indicated that important risk factors for malaria include advanced vulnerability in males, individuals with lower educational stages, and those with poor shelter conditions such as roof space and wall holes. Moreover, absence of bed net manipulation, proximity to cattle, and intimacy to mosquito breeding spots were significant threat factors (47).

According to a study done in the Ethiopian city of Mizan-Aman, malaria was more prevalent in those aged 25 to 34 (5.8%); providing health education that enhances people's knowledge of the illness and transforms community activities related to ITN operations may aid in attempts to stop the disease's spread(48).

2.3. Effects of Malaria on Coagulation Profiles

A prospective observational study at a tertiary care center in India showed that 72% of malaria patients had abnormalities in coagulation parameters. Specifically, PT was increased in 22% of cases, APTT in 14%, bleeding time (BT) in 5%, and 4% of patients exhibited bleeding manifestations (14). Another study in India reported a significant positive correlation between the level of parasitemia and increased PT, indicating that higher parasite loads are associated with longer clotting times (16).

A cross-sectional observational study conducted in a tertiary health care institute in Ghaziabad revealed that among 100 malaria patients, anemia was present in 62% (including 14% with severe anemia), low platelet counts in 63% (with 25% severe in mixed infections), and prolonged coagulation times 22% with increased PT and 14% with increased APTT (51). A study at the Department of Pathology, Military Hospital Lahore, found that *P. falciparum* was responsible for the remaining malaria cases, with *P. vivax* accounting for more than 60% of cases. While normal coagulation profiles were observed in *P. vivax* patients, *P. falciparum* infections were associated with increased clotting potential (52).

An open-label randomized study conducted in Germany on controlled human malaria infection (CHMI) revealed an increase in thrombin generation potential by 17.7% at very early stages of *P. falciparum* malaria. This suggests a hypercoagulable state may be induced, even with low parasite density, potentially providing a more sensitive tool for early diagnosis (53). A cross-sectional study at the Military Hospital Lahore, Pakistan, found that partial thromboplastic time (PTT), APTT, and D-dimer levels were positively correlated with parasitemia, particularly in *Plasmodium falciparum* infections (54).

In Surat, Gujarat, a cross-sectional study showed that PT was increased in 21.15% of cases, APTT in 14.42%, and BT in 7.5% of patients with P. falciparum. Out of these, 5% had bleeding manifestations (15). A case-control study conducted in Sudan compared young malaria patients under 5 to healthy children. It found that malaria significantly disrupts both blood cell counts and clotting factors, with malaria patients showing lower red blood cell counts and higher clotting times (APTT and PT), suggesting an increased risk of clotting complications (55).

A study in Nigeria revealed significant prolongation of PT and APTT in symptomatic malaria patients compared to asymptomatic ones, along with a statistically significant decrease in platelet counts (56). A cross-sectional study conducted in Ahlia, Sudan, found that prothrombin time was prolonged in 22.9% of falciparum malaria cases, with prolonged partial thromboplastic time observed in 4.2% of cases and elevated D-dimer levels indicating coagulation activation. High parasitemia correlated with more severe coagulation abnormalities (57).

A hospital-based case-control study in Sudan showed that the most common coagulation abnormalities were increased PT, APTT, and TT, indicating slow blood clotting. Additionally, 95% of malaria patients had low platelet counts, and 97% had impaired platelet aggregation (58). Another hospital-based case-control study in Sudan suggested that malaria primarily affects the extrinsic clotting pathway (measured by prolonged PT), while the intrinsic pathway (measured by APTT) remains unaffected. The degree of parasitemia did not correlate with PT, APTT, or age (59).

APTT increased in 20% of patients with P. falciparum and mixed infections. Mild parasitemia was associated with a 0.002%-0.199% increase in PT. Increasing parasitemia was positively correlated with alterations in PT, with significant findings related to the degree of parasitemia(16).

Consumptive coagulopathy and the development of DIC are caused by accelerated turnover of the coagulation cascade caused by malaria infection; PT and APTT were prolonged in 47.5% and 35% of cases, respectively, showing significant elongation in affected individuals (62). The result of the study showed that malaria infection debilitates prothrombin time by causing prolongation in prothrombin time. This is in line with this effect; therefore, it is an indication that malaria patients may have a deficiency of factors I, II, VII, and X when it is prolonged (56).

2.4. Diagnostic Value of Selected Hematological Parameters in Predicting Severity of Malaria

A case-control study in Cameroon emphasized significant hematological changes in malaria-infected cases, including reduced situations of hemoglobin, white blood cells, and platelets. These findings emphasize the diagnostic value of these hematological parameters in detecting malaria (34).

At Pho Phra Hospital in Thailand, investigation showed that low platelet counts, among other blood parameter changes, are helpful indicators for diagnosing malaria, especially in indigenous areas. Thrombocytopenia was distinguished for its high sensitivity and possible to enable fast diagnosis, even at low parasite levels (18).

A cross-sectional study in Accra, Ghana, revealed that increasing parasite levels in malaria cases were associated with raised WBC counts but reduced levels of red blood cells, hemoglobin, platelets, and other red blood cell indicators. This pattern, probably due to parasite destruction and immune reactions, emphasizes the significant hematological impact of malaria infection (19).

In Mumbai, India, a case-control study assessed hematological parameters for diagnosing and distinguishing malaria, particularly *Plasmodium vivax*, from other infections, for instance, dengue. The study observed thrombocytopenia and abnormal WBC count peaks in histograms as possible diagnostic markers for malaria (63).

Another case-control study in Mumbai realized that severe malaria induces significant blood cell abnormalities, which can be crucial for diagnosis and monitoring. But the fundamental mechanisms of these hematological changes remain largely unexplored (35). A controlled trial study in Pakistan reported that malaria cases showed lower levels of hemoglobin, PCV, albumin, and glucose, while having advanced levels of ESR, platelets, creatinine, urea, and white blood cells compared to healthy individuals (64).

Malaria infection repeatedly leads to thrombocytopenia, a drop in platelet counts below 150,000/μL. Multiple causes are suspected in the destruction of platelets in circulation, changes in bone marrow production, extreme elimination by the spleen, consumption during blood clotting complications, and indeed clumping of infected red blood cells that masks exact platelet numbers (32).

The possibility to diagnose unknown cases of malaria for patients exposed to complete blood count (CBC) is one of the main benefits of flagging malaria in hematology analyzers (63). A cross-sectional health facility-grounded study conducted at Ataye District Hospital in Ethiopia demonstrated that thrombocytopenia is an extremely effective discriminatory test for malaria, with 79.5% sensitivity and 86.3% specificity (20).

In Harar, Ethiopia, an institutional comparative cross-sectional study found that patients with malaria had significantly lower platelet counts, plateletcrits, and mean platelet volumes than healthy adults; malaria parasitemia also showed a weak positive correlation with mean platelet volume and a moderate inverse correlation with platelet count(62).

2.5. Conceptual framework

The study considered socio-demographic, coagulation profiles, hematologic profiles, clinical characters, behavioral, and environmental factors. These factors have a direct relationship with malaria. The conceptual framework below has been derived from different reviewed literatures (15,21,48,54) (Figure 1).

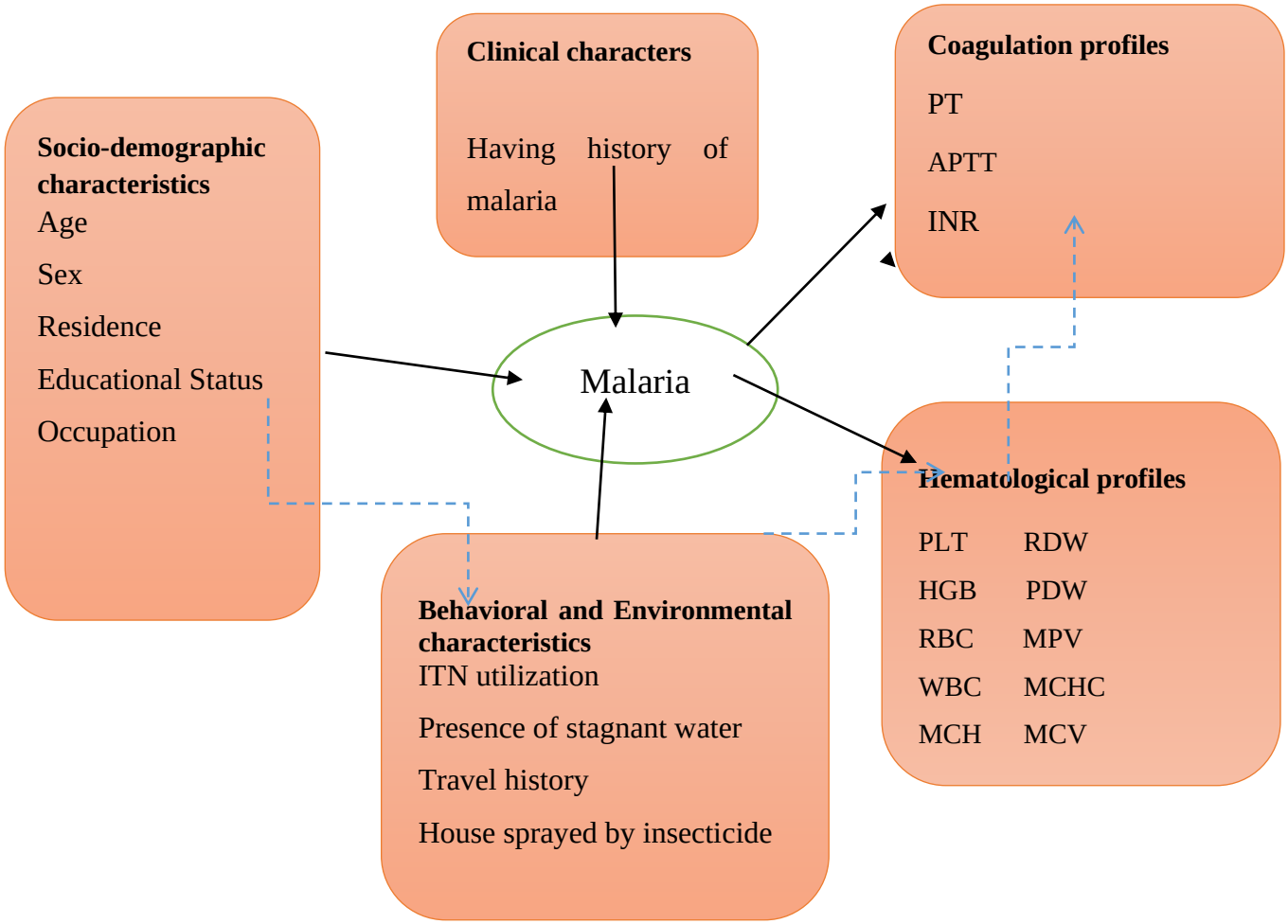

Figure 1.Conceptual framework illustrating how dependent and independent variables relate to one another

(Source: prepared by the principal investigator after revising different literatures).

→ The solid line shows how the components are related, as well as how interested this study is in seeing these relationships.

⇢ The broken line shows the relationships between the factors; however, our study is not interested in seeing these relationships.

3. MATERIALS AND METHODS

3.1. Study Area

This thesis was conducted at WKUSTH; a healthcare service located about 158 kilometers from Addis Ababa, the capital of Ethiopia. The city has an elevation between 1910 and 1935 meters above sea level (29). The hospital was found in the Gubriye sub-city in the Gurage zone, Central Ethiopia. The hospital delivers services for over 1.2 million people living in the Gurage zone and the neighboring area.

WKUSTH offers chronic care, NICU, emergency services, ART services, surgical, dental, and medical services; ophthalmology; pediatrics; gynecology; radiology; physiotherapy; pathology services; pharmacy; and laboratory services (65). And also, WKUSTH involves 641 health professionals and other administrative staff serving in numerous departments.

3.2. Study Period and Design

- The study was carried out from February to April 2024 using a cross-sectional study design.

3.3. Population

3.3.1. Source Population

- All adult patients who develop acute febrile infection at WKUSTH.

3.3.2. Study Population

- All adult patients who were suspected of having malaria at WKUSTH during the study period, in central, emergency, and inpatient.

3.4. Inclusion and Exclusion Criteria

3.4.1 Inclusion Criteria

- All malaria suspected adult patients aged 18 and above years old were included in the study to minimize information bias related to age (66).

3.4.2 Exclusion Criteria

- The exclusion criteria were developed based on WHO guidelines (67,68). Malaria suspected participants were excluded if they met any of the following conditions.
  - ✓ Currently receiving anti-malarial therapy.

- ✓ Currently receiving anticoagulant therapy.
- ✓ Currently receiving antiretroviral therapy (ART).
- ✓ History of anemia, leukemia, coagulation disorders, liver disease.

3.5. Variable of the Study

3.5.1 Dependent Variable

- Malaria

3.5.2. Independent Variable

- Socio-demographic variable
  - ✓ Age
  - ✓ Gender
  - ✓ Residence
  - ✓ family size
  - ✓ Educational status
  - ✓ Occupational status
- Environmental and Behavioral Factors:
  - ✓ Previous history of malaria
  - ✓ ITN usage
  - ✓ Staying night outdoor
  - ✓ Presence of stagnant water near to home
  - ✓ Travel history
  - ✓ Indoor residual spray (IRS)
  - ✓ Presence of hole in wall and roof of house

3. 6. Sampling Size and Sampling Techniques

3.6.1. Sample size calculation

The single population proportion formula was used to calculate the sample by considering the following hypotheticals: anticipated frequency (the prevalence of malaria patients and marginal error of 5%). The overall frequency of malaria is 24.7% (47). In conclusion, a population correction formula was employed.

$$n = \frac{(Za/2)^2\, p(1-p)}{(d)^2}$$

where:

n is the desirable sample size.

z is the z-score for the required confidence level (1.96 for 95% confidence).

p-value is anticipated frequency of malaria = 24.7% = 0.247

d is the required margin of error = 0.05

$$n = \frac{(1.96)^2\, 0.247(1-0.247)}{(0.05)^2} = 286$$

Therefore, the final sample size for the study was 286.

3.6.2. Sampling technique

- Participants in the study were chosen at WKUSTH using the consecutive sampling technique.

3.7. Data Collection Tools

In order to collect data on malaria findings, data collection tools were planned as follows:

3.7.1. Questionnaire Survey

The types of data that were collected by a pretested structured questionnaire include sociodemographic (age, gender, residence, education, occupation, travel history, malaria history, bed net use, and preventive medication adherence). Before beginning data collection, data collectors chose participants who met the inclusion requirements, used a checklist model to exclude study participants who did not fulfill them, and obtained consent from each study participant.

The questionnaire was developed based on existing published literature reviews (15, 21, 48, 54)by the principal investigator, potentially collaborating with medical professionals and cultural experts in the English language and translated into Amharic, the local language, for cultural sensitivity and accessibility.

The data collectors were trained personnel who administered the questionnaire using standardized interview techniques, ensuring consistency and participant comfort, and the principal investigator, who supervised data collection, maintained quality control and addressed any issues.

To ensure clarity, understandability, and relevance, the questionnaire was undergoing a pretest with a representative 5% group at Attat Primary Hospital. The pretest was conducted with approximately 14 participants from the total sample size of 286. Feedback from this pre-test was used to revise the questionnaire for improved quality and reliability.

3.7.2. Laboratory Analysis

3.7.2.1. Sample collection and processing

Samples of capillary and venous blood were obtained from malaria suspected patients. Each patient's capillary blood was obtained by puncturing their left ring finger with a sterile blood lancet. The blood was collected with a sterile pasture pipette after cleaning the first flow of blood. To detect plasmodium species, both thin and thick films were made.

Additionally, a skilled laboratory technologist and the principal investigator followed normal operating protocols to obtain five milliliters of venous blood. Two test tubes were assigned to the acquired blood sample. In order to analyze the PT, APTT, and INR tests, the first 2.7 mL was transferred to a test tube that was ant-coagulated with 3.2% sodium citrate.

The remaining volume of blood was transferred to K3 EDTA test tubes for complete blood count (CBC) via the Zybio Z30 hematology analyzer that uses flow cytometry to measure blood cell characteristics. As soon as the tube was flipped eight times, the blood was combined with anticoagulant and labeled. In order to get platelet-poor plasma (PPP) for the PT, INR, and APTT tests, blood containing citrated anticoagulant was spun for 15 minutes at 1500 revolutions per minute. Then PT, APTT, and INR were measured using the Urit 610 coulometer analyzer. The test was done at the central emergency and impatient laboratory of WKUSTH.

From capillary blood obtained by finger puncture using a sterile lancet, both thick and thin blood smears were prepared on a frosted microscope slide for every acute fever patient. Absolute methanol was used to fix the thin blood film after it had been allowed to air-dry at ambient temperature. Next, a skilled medical laboratory technologist viewed the blood film using a 100× oil immersion objective after staining it for 10 minutes with 10% Giemsa solution(69).

A 100X objective lens was used to examine at least 100 fields in order to determine whether plasmodium species were present. If no parasites were found during this examination, the test was considered negative. Thin blood smears were used to identify malaria species while thick smears were utilized to detect and quantify parasites. The number of asexual parasites (both trophozoite and schizont phases of malaria) and 200 WBC were used to measure malaria parasitemia in thick film. To determine the amount of malaria parasitemia, which is measured by the number of asexual parasites per microliter of blood, the number of asexual parasites was divided by the number of white blood cells (WBCs) detected. The result was then multiplied by the number of WBCs per microliter of blood. Calculated by using the formula:

Parasite / µL = Parasite counted / 200 WBC × Total WBC count

3.8. Data Analysis

All data collected from the questionnaires throughout the study period were coded, cleaned, and entered using Epidata 3.1 and then exported to the Statistical Package for the Social Sciences (SPSS) version 26.0 for additional analysis. Descriptive statistics, as well as frequency distributions, mean, median, and standard deviation, were calculated.

Upon accomplishment of data entry, a detailed cross-check was conducted between the electronic and paper forms to confirm reliability and diminish errors. After this cross-check, the data were cleaned to address missing values, outliers, and inconsistencies. Binary logistic regression, Mann-Whitney U test, and ROC curve analyses were executed.

The data in this study were not normally distributed, because the Kolmogorov-Smirnov and Shapiro-Wilk tests ($p < 0.05$) for CBC and coagulation variables. Therefore, the Mann-Whitney U test was selected to compare the distribution of CBC and coagulation profiles in the malaria-positive and negative groups. This test is used to compare and contrast the medians of two independent groups. ROC curve analyses were selected to identify the best diagnostic values from selected hematological profiles to predict the severity of malaria. Results were considered statistically significant when the P-value was less than or equal to 0.05.The Hosmer-Lem show test was used to measure the appropriateness of the model. The results were offered using tables, figures, text, and ROC curves.

3.9. Data Quality Control

In order to maintain the quality of the data, the data collectors received one day of training on how to gather, process, and record samples. Data collectors and major investigators were under constant supervision. To guarantee that the parasite counts were correct, two certified lab technologists examined each slide independently. The parasite densities were then calculated by averaging the two counts.

In order to check the quality control of the examined slides, quality control measures were implemented. Initially, each slide was independently reviewed by a second, experienced medical laboratory technologist to verify the findings. Discussion and agreement were used to resolve any differences between the two evaluations.

In addition, a random subset of slides was selected for re-examination to assess consistency in results. The staining process was carefully monitored to ensure proper preparation and application of the 10% Giemsa solution, adhering to the recommended staining time of 10 minutes. Likewise, the quality of reagents, such as Giemsa stains, was also examined using known positive and negative samples before beginning work on a new batch of Giemsa.

Through strict adherence to laboratory standard operating protocols, the quality of test results was preserved. A regular background check was carried out to lower background error for the hematologic profile count. Each process was evaluated and routinely examined by the investigator to ensure the accuracy and completeness of the data gathered. Throughout the investigation, these combined actions assisted in preserving the data's quality control.

3.10 Ethical Considerations

The thesis was carried out with ethical consent from the School of Medical Laboratory Sciences' Research and Ethics Committee. Wolkite University also provided a letter of support. Each subject gave their informed consent before the study started.

The goals, advantages, and possible hazards of the study were all explained in detail to the participants. Additionally, ethical clearance letter from Wolkite University was acquired, attesting to the voluntary nature of participation.

3.11. Dissemination of Result

The thesis findings will be presented to Wolkite University College of Medicine and Health Sciences' Department of Medical Laboratory Sciences. A copy will be given to WKUSTH as well. Presentations of the findings will be attempted at conferences, meetings, workshops, and seminars both domestically and abroad. The research findings' publishing will also be taken into account.

4. RESULT

4.1. Socio-Demographic Characteristics of the Study Participants

Of the 286 adult patients who took part in the study, 115 (40.2%) were male and 171 (59.8%) were female. The study's participants were between the ages of 18 and 64; their average age was 35.13 years, with a standard deviation of 11.094 years. Of the adult patients, the largest group 87 (30.4%) patients were between the ages of 28 and 37, followed by 80(28%) patients in the 18 to 27 age range, 83(29%) patients in the 38 to 47 age range, 24(8.4%) patients in the 48 to 57 age range, and 12(4.2%) patients in the 58 to 65 age range.

Of the adult patients, 154 (53.8%) were from urban, leaving the remaining patients from rural areas. Of the participants, 155 (54.2%) had a family size of fewer than five people. 73 (25.5%) of the respondents had a diploma, which was the majority in terms of educational standing. Of the 286 individuals, 110 (38.5%) were government workers (Table 1).

Table 1: Socio-demographic characteristics of adult patients at Wolkite University Specialized Teaching Hospital (WKUSTH), Wolkite, Central Ethiopia, from February-April 2024

Variable	Category	Frequency	Percentage
Age in years	18-27	80	28
	28-37	87	30.4
	38-47	83	29.0
	48-57	24	8.4
	58-65	12	4.2
Gender	Female	171	59.8
	Male	115	40.2
Residence	Urban	154	53.8
	Rural	132	46.2
Family size members	<5	155	54.2
	≥5	131	45.8
Educational status	Unable to read and write	62	21.7
	Primary	44	15.4
	Secondary	63	22.0
	Diploma	73	25.5
	Degree and above	44	15.4
Occupational status	Farmer	65	22.7
	Daily laborer	29	10.1
	Government	110	38.5
	Merchant	58	20.3
	Student	24	8.4

4.2. The prevalence of malaria and dominant Plasmodium species

It was shown that 41(14.3%) of the study participants had malaria overall. Of the adult patients with the infection, 28 (68.3%) had *P. vivax*, whereas 13 (31.7%) had *P. falciparum*(Figure 2).

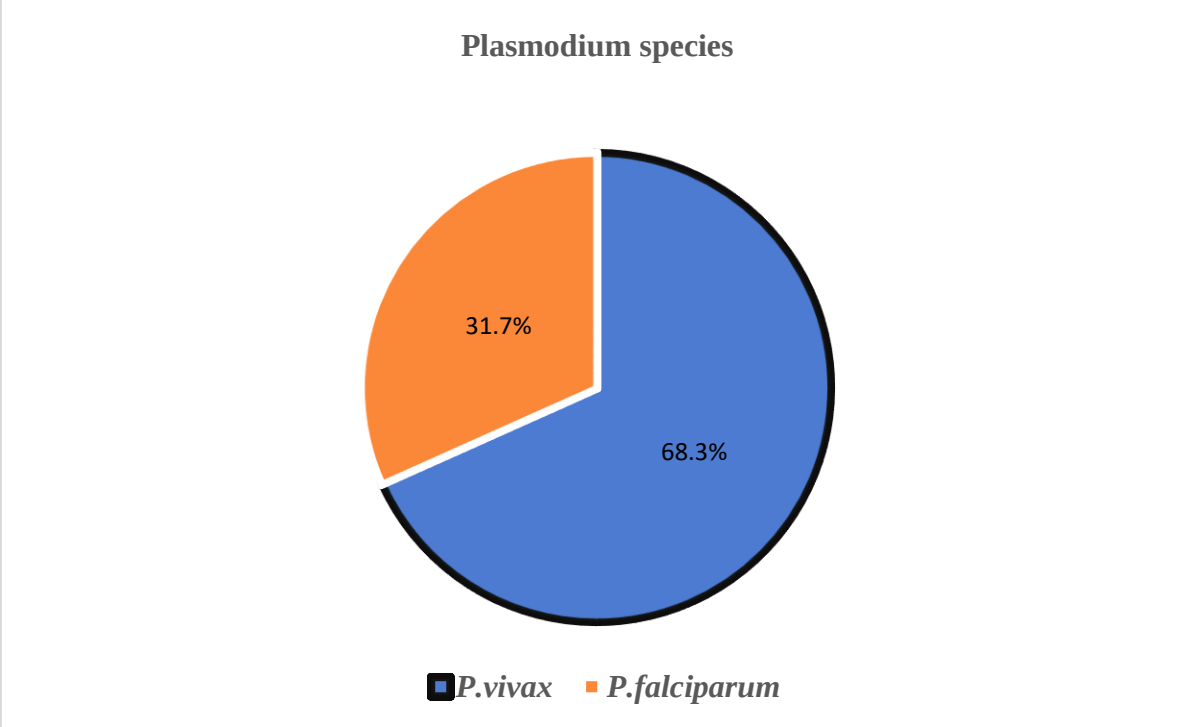

Figure 2. Plasmodium species distribution among adult patients at WKUTSH, Wolkite, Central Ethiopia, from February-April 2024

4.3parasitic density of malaria parasite

The lowest and largest parasite densities were 160 and 14,000 parasites/µl of blood, respectively, whereas the geometric mean parasite density was 3363.41 parasites/µlof blood. The parasite densities ofmildparasitemiaaccounted for 26 (63.4%), moderate 10 (24.4%), severe 5 (12.2%) of the total parasite density (Figure 3).

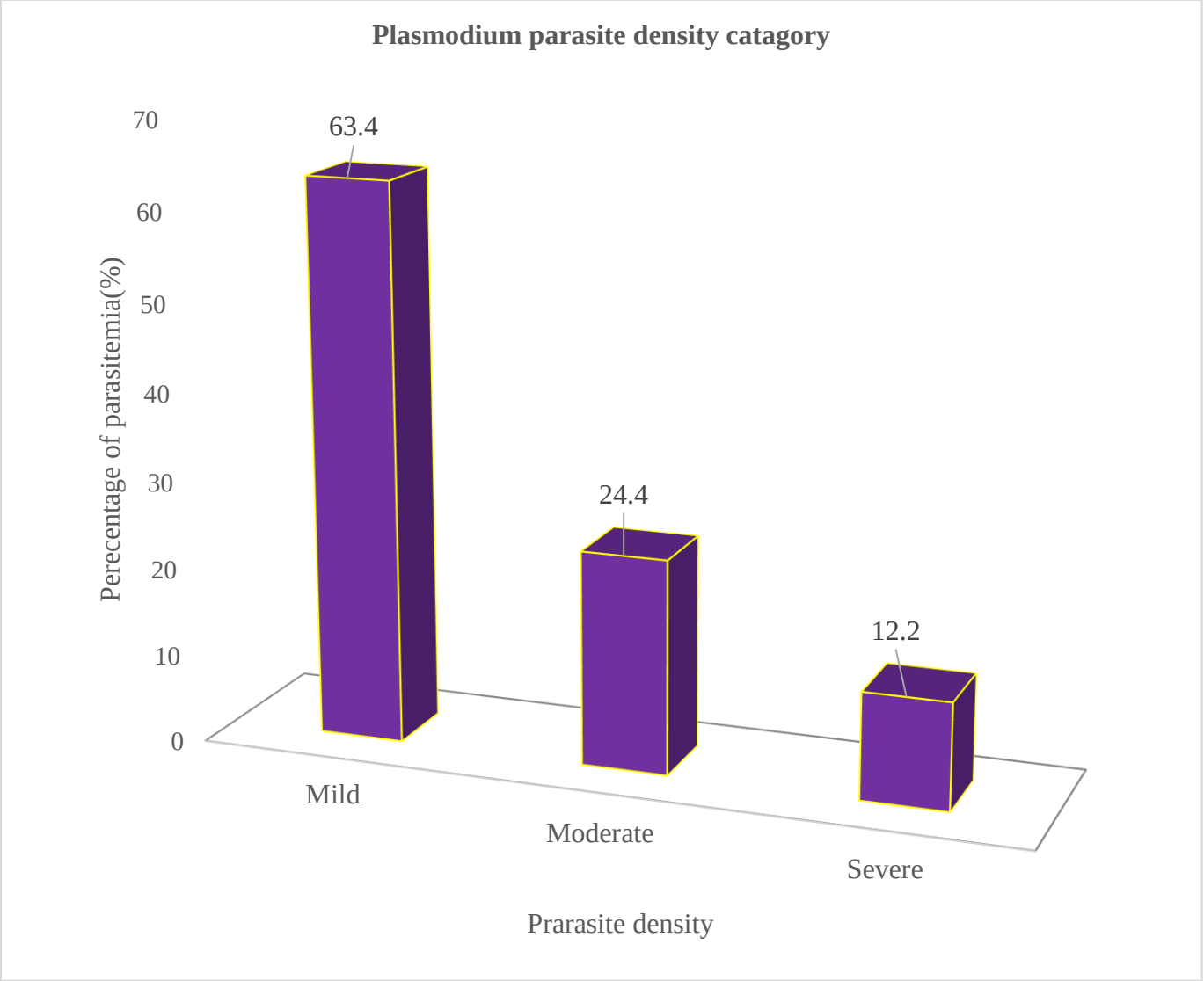

Figure 3.Plasmodium parasite density distribution among adult patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024.

4.4. Associated factors of malaria

To analyze all possible components associated with malaria, bivariate logistic regression was used. Bivariate logistic regressions showed no statistically significant association between the respondents' age, gender, place of residence, family size, and presence of holes in the walls and roof of the house.

On the other hand, factors associated with malaria ($P < 0.05$) included previous malaria history, using an ITN, staying the night outside, having stagnant water near to the house, and travel history. To adjust for possible confounding factors, a multivariate logistic regression model was applied to all variables with a P-value of less than 0.25. Gender, family size number, and the presence of holes in the wall or roof of the house, was not found to be associated after adjustment ($P > 0.05$). Age and place of residence were not candidate variables for a multivariate logistic regression model.

An adjusted logistic regression analysis showed adult study participants with a previous history of malaria had a 3.7-fold increased risk of *plasmodium* parasite infection compared to those without a history (AOR = 3.724, 95% CI = 1.316-10.537).

When compared to adult study participants who did not use ITN, those who used ITN encountered a 6.2-fold lower risk of having a Plasmodium infection (AOR=6.208, 95%CI=2.380-16.191). Patients who stayed out the night had a 4.5-fold higher risk of *plasmodium* parasite infection compared to those who did not (AOR = 4.505, 95% CI = 1.677-12.06).

The chance of having malaria is 4.1 times higher in areas with stagnant water than in areas without malaria (AOR = 4.118, 95% CI = 1.801-9.413). Travel history was also a prominent risk factor, with adults who had traveled being 3.4 times more likely to infect *plasmodium* parasites as compared to those who did not (AOR = 3.365, 95% CI = 1.238-9.146)(Table 2).

Table 2: Bivariate and multivariate analysis of associated risk factors for malaria among adult patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024

Associated factors		Malaria status					
		Positive n (%)	Negative n (%)	COR (CI)	P-value	AOR (CI)	P-value
Age	18-27	12(29.3)	68(27.8)	1			
	28-37	15(36.6)	72(29.4)	1.181(0.516 -2.703)	0.694		
	38-47	10(24.4)	73(29.8)	0.776(0.315-1.913)	0.582		
	48-57	4(9.8)	20(8.2)	1.133(0.329-3.903)	0.843		
Gender	Female	19(46.3)	152(62)	1		1	
	Male	22(53.7)	93(38)	1.892(0.972-3.683)	0.060	1468(658-3278)	0.348
Residence	Urban	21(51.2)	133(54.3)	1			
	Rural	20(48.8)	112(45.7)	1.131(0.583-2.192)	0.716		
Family size members	<5	26(63.4)	129(52.7)	1			
	≥5	15(36.6)	116(47.3)	0.642(0.324-1.270)	0.203	0.501 (0.220-1.145)	0.101
History of malaria *	Yes	35(85.4)	150(61.2)	3.694(1.497-9.117)	0.005	3.724(1.316-10.537)	0.013*
	No	6(14.6)	95(38.8)	1		1	
ITNs usage*	Yes	23(56.1)	214(87.3)	1		1	
	No	18(43.9)	31(12.7)	5.403(2.623-11.129)	0.000	6.208(2.380-16.191)	0.000*
Staying night outside*	Yes	32(78)	116(47.3)	3.954(1.811-8.633)	0.001	4.505(1.677-12.106)	0.003*
	No	9(22)	129(52.7)	1			
Presence of house hole	Yes	34(82.3)	177(72.2)	1.866(0.789-4.411)	0.155	0.841(0.300-2.354)	0.741
	No	7(17.1)	68(27.8)	1		1	
Presence of stagnant water *	Yes	22(53.7)	37(15.1)	6.509(3.212-13.193)	0.000	4.118(1.801-9.413)	0.001*
	No	19(46.3)	208(84.9)	1		1	
Travelling history*	Yes	35(85.4)	110(44.9)	7.159(2.905-17.642)	0.000	3.365(1.238-9.146)	0.017*
	No	6(14.6)	135(55.1)	1		1	

* Statically significant variables; AOR = Adjusted Odds Ratio; COR= Crude Odds Ratio; CI = Confidence Interval; ITN = Insecticide-Treated Bed Net.

4.5. Coagulation and hematologic profiles of malaria-infected patients

This study found that significant differences in coagulation and hematologic profiles exist between malaria-infected and malaria non-infected patients. PT is notably prolonged in malaria-infected patients, with a median of 15.9 seconds compared to 13.1 seconds in malaria non-infected patients, and this difference is statistically significant (p =0.001).

Similarly, the INR is higher in malaria infected patients (1.27) than in malaria non-infected patients (1.09), with a p-value of 0.001, indicating a clear impact of malaria blood film positivity on coagulation. The APTT is also elevated in malaria infected patients, with a median of 37 seconds compared to 29.1 seconds in malaria non-infected patients, and this result is statistically significant (p = 0.001).

Hematologic parameters further highlight differences between the two groups. The median of WBC count is significantly higher in malaria-infected patients (9.49 x 10^3/µL) compared to malaria non-infected patients (6.18 x 10^3/µL), with a p-value of = 0.001.

The neutrophil count is also elevated in malaria infected patients (6.1 x 10^3/µL) relative to non-infected ones (4.1 x 10^3/µL), and this difference is significant (p = 0.001). Basophil counts are higher in malaria infected patients (0.03 x 10^3/µL) compared to non-infected patients (0.01 x 10^3/µL), with a p-value of 0.001, indicating a notable difference. Monocyte counts are also higher in malaria-infected patients (0.76 x 10^3/µL) compared to non-infected patients (0.36 x 10^3/µL), showing a highly significant difference (p = 0.001).

In terms of RBC count and HGB levels, malaria-infected patients have a lower median RBC count (4.20 x 10^6/µL) and HGB level (10.9 g/dL) compared to malaria non-infected patients, whose RBC count is 4.39 x 10^6/µL and HGB level is 12.2 g/dL. The differences are statistically significant, with a p-value of 0.001 for both measures.

The study demonstrated a significant difference in MCV and MCH between malaria-infected and non-infected patients. Malaria-infected individuals exhibited significantly reduced levels of both MCV (88.2 fl versus 90.8fl) and MCH (28.9 pg versus 29.8 pg) compared to non-infected individuals.

PLT is significantly reduced in malaria-infected patients (148 x 10^3/µL) versus malaria-non-infected patients (240 x 10^3/µL), with a highly significant p-value of 0.001. Additionally, the MPV is increased in malaria-infected patients (11 fL) compared to non-infected (9.8 fL), with a p-value of = 0.001. The study found a significant difference in both PDW and RDW among malaria-infected and non-infected individuals. Malaria-infected patients showed significantly higher levels of PDW (16.4%, p=0.000) and RDW (14.1 fl, p=0.001) compared to non-infected patients (PDW= 15.7%, RDW=13.1 fl).

There was no significant difference in the median of lymphocyte and MCHC between the two groups with p-value > 0.05. Overall, these findings suggest that patients with malaria were associated with significant alterations in coagulation and hematologic profiles, including prolonged coagulation times, elevated WBC count and differential counts, reduced HGB, MCV, MCH, and PLT counts, increased MPV, PDW, and RD (Table 3).

Table 3: Comparison of coagulation and hematologic profiles between patients with malaria and Patients without malaria groups at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024

Variable	Patients with malaria	Patients without malaria	P-value
	Median [IQR]	Median [IQR]	
PT/seconds	15.9 [1.90]	13.1 [1.70]	P = 0.001
INR/seconds	1.27 [0.15]	1.09 [0.12]	P = 0.001
APTT/seconds	37 [3.40]	29.1 [5.74]	P = 0.001
WBC x103/ µL	9.49 [6.77]	6.18[2.88]	P = 0.001
Neutrophil x103/ µL	5.56 [5.36]	3.75 [2.04]	P =0.001
Eosinophil x103/ µL	0.06 [0.11]	0.01 [0.02]	P= 0.010
Basophil x103/ µL	0.03 [0.09]	0.01 [0.02]	P =0.001
Lymphocyte x103/ µL	1.73 [1.46]	1.69 [0.77]	P = 0.633
Monocyte x103/ µL	0.76 [0.75]	0.36 [0.26]	P = 0.001
RBC x106/ µL	4.20 [0.82]	4.39 [0.65]	P = 0.001
MCV (fl)	88.2 [7.5]	90.8 [5.9]	P = 0.025
MCH (pg)	28.9 [2.10]	29.8 [2.4]	P = 0.032
MCHC (g/dl)	32.9 [1.0]	33.1 [1.85]	P = 0.727
HGB (g/dl)	10.9 [2.45]	12.2 [1.85]	P = 0.001
PLT x103/ µL	148 [68.0]	240 [76.00]	P = 0.001
MPV (fl)	11 [3.00]	9.8 [2.00]	P = 0.001
PDW (%)	16.4 [1.45]	15.7 [1.20]	P = 0.001
RDW (fl)	14.1 [2.20]	13.1 [1.30]	P = 0.001

PT =Prothrombin Time, INR= International Normalized Ratio, APTT= Activated Partial Thromboplastic Time, PLT=Platelet count, MPV= Mean Platelet Volume, PDW = Platelet Distribution Width RDW = Red Cell Distribution Width, IQR=Interquartile Range.

4.6. The diagnostic value of selected hematological profiles for predicting malaria

The diagnostic value of the selected hematological profiles in predicting the severity of malaria was determined by using ROC curve analysis. The diagnostic value of various hematologic profiles in distinguishing between malaria-positive (MP) and malaria-negative (MN) patients was assessed for sensitivity, specificity, cut-off values, and the area under the curve (AUC) with associated confidence intervals (CI) and p-values.

The monocyte count shows the highest sensitivity at 97.6%, indicating it very effective at correctly identifying MP patients. It also has a high AUC of 0.864, suggesting excellent overall value in distinguishing between MP and MN patients. Similarly, the RDW and PDW both achieve a sensitivity of 97.6% with AUC values of 0.775 and 0.757, respectively, which also indicates strong diagnostic capability.

The MPV and WBC count demonstrate slightly lower sensitivities of 90.2% and 87.8%, respectively, but still show substantial diagnostic value with AUCs of 0.707 and 0.701. All profiles are statistically significant ($p < 0.001$), confirming their reliability in differentiating malaria-positive from malaria-negative patients (Table 4 and Figure 4).

Table 4: Diagnostic value of selected hematologic profiles for predicting malaria-positive (MP) from malaria-negative (MN) adult patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024

Hematologic Profile	Sensitivity (%)	Specificity (%)	Cut off value	AUC	95% CI	P-value
Monocyte x103/µL	97.6	80.8	0.245	0.864	0.786 - 0.942	< 0.001
RDW (%)	97.6	79.6.	12.35	0.775	0.695 -0 .855	< 0.001
PDW (fl)	97.6	78.0	14.85	0.757	0.670 -0 .844	< 0.001
MPV (fL)	90.2	82.4	8.55	0.707	0.610-0 .804	< 0.001
WBC x103/µL	87.8	80.0	4.425	0.701	0.599 -0.803	< 0.001

AUC=Area under curve, RDW= Red cell distribution width, PDW= Platelet distribution width, MPV=Mean platelet volume

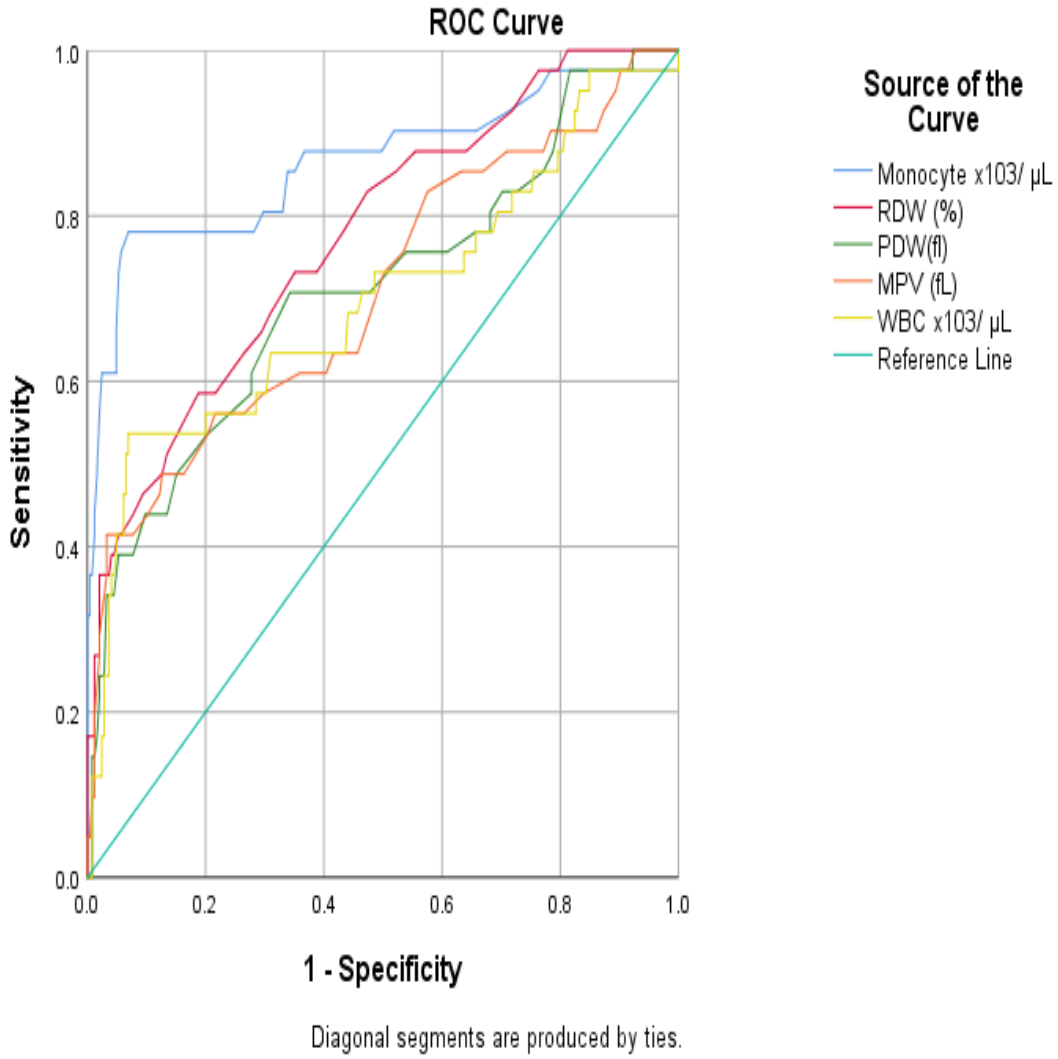

Figure 4: ROC curve analysis of selected hematologic profiles for predicting malaria-positive (MP) from malaria-negative (MN) adult patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024.

In distinguishing malaria-complicated (MC) from malaria-uncomplicated (MU) patients, the monocyte count demonstrates a sensitivity of 88.9% and specificity of 87.5%, with an AUC of 0.755, indicating best ability to differentiate between MC and MU patient (Table 5 and figure 5).

Table 5: Diagnostic value of selected hematologic profiles for predicting malaria-complicated (MC) from malaria-uncomplicated (MU)patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024

Hematologic Profile	Sensitivity (%)	Specificity (%)	Cut off value	AUC	95% CI	P- value
Monocyte x103/ µL	88.9	87.5	0.4050	0.755	0.508-1.002	= 0.043

MC= Includes Sever malaria, MU= Includes mild and moderate malaria,
AUC=Area under Curve

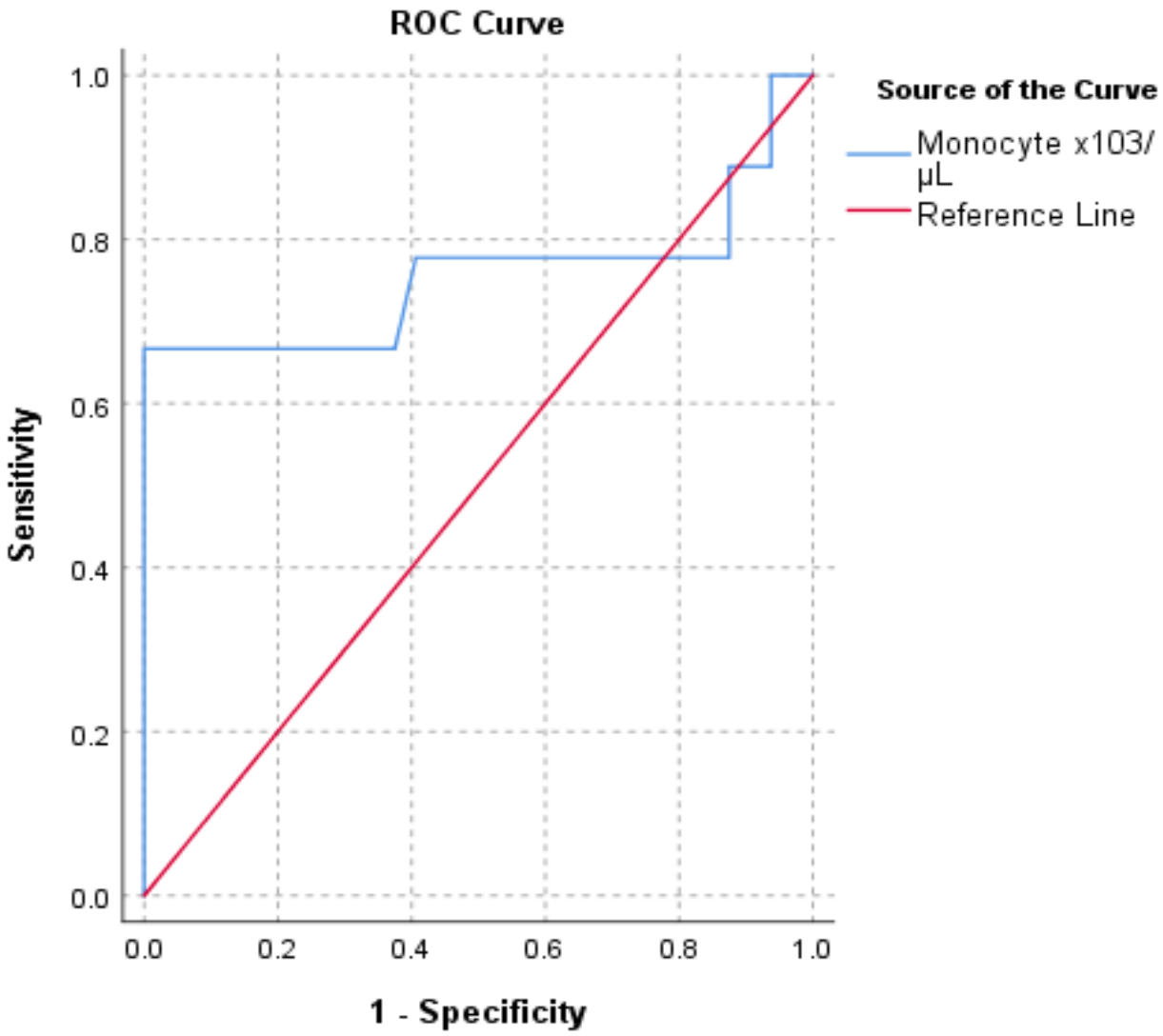

Figure 5: Diagnostic value of selected hematologic profiles for predicting malaria-complicated (MC) from malaria-uncomplicated (MU)patients at WKUSTH, Wolkite, Central Ethiopia, from February-April 2024.

5. DISCUSSION

Malaria is a disease that is prevalent in underdeveloped countries. Ethiopia is one of the sub-Saharan countries extremely endemic to malaria, where nearly 68% of the population survives in malaria's area (20).The current study observed a *Plasmodium* infection prevalence of 14.3% (95% CI = 10.5-18.5) among adults at Wolkite University Specialized Teaching Hospital, moderate transmission areas (36).

This result is analogous to a 14.3% prevalence reported from in Tanzania (70). The result was lower than 33.6% in Sabah, Malaysia (40), 55% in Ibadan, southwestern Nigeria (71), 19.7% in Bossaso, Somalia(43), 24.7% in Lake Tana, Ethiopia (47), and 22.4% in the Dembiya district of Northwestern Ethiopia (45). Nonetheless, our study's malaria prevalence was greater than the 8.7% found in Northwest Ethiopia's Wogera district(46). The reasons for differences in malaria prevalence could be seasonal variation, study period, differences in altitude, and ITN usage can also affect results (72).

Wolkite, situated at an altitude of 1910 to 1935 meters above sea level, experiences moderate malaria transmission, primarily influenced by seasonal climatic variations (29). This altitude places it within a transmission zone where malaria prevalence is expected to be lower compared to regions at lower elevations. For instance, Ibadan in Nigeria, situated at much lower altitudes of 200–300 meters, has a much higher malaria prevalence of 55% (71), reflecting the greater mosquito vector activity that is facilitated by warmer temperatures and consistent rainfall at lower altitudes.

In comparison, Wogera, located in the Amhara Region at a higher altitude of greater than 2050 meters above sea level, reported lower malaria prevalence of 8.7% (46). The cooler temperatures at this higher altitude likely contribute to the reduced transmission of malaria in Wogera. In this investigation, *P. vivax* was the most common Plasmodium parasite found (68.3%), followed by *P. falciparum* (31.7%). This finding is similar to previous studies conducted in Butajira(72), Shewa Robit (73), and Halaba (74). The increase in *P. vivax* malaria can be attributed to various biological and genetic factors.

Biological factors may include shorter sporogony periods, allowing for quicker infection cycles; the presence of hypnozoites enables latent infections, contributing to disease reappearance (72). Genetic factors may also include the Duffy antigen receptor chemokines (DARC) on red blood cells that act as a gateway for *P. vivax* merozoites; therefore, individuals with DARC (Duffy-positive) are more susceptible to *P. vivax* than those without DARC (Duffy-negative) (75).

The analysis of parasite density categories revealed that the majority of participants (63.4%) had mild malaria infections, characterized by low parasite loads. Moderate infections were observed in 24.4%, while severe infections were the least, 12.2% of the sample. This finding is in line with research conducted in the Boset District in the East Shoa Zone, Oromia Region, Ethiopia(76).

The predominance of mild malaria infections is largely due to the development of partial immunity in long-term residents of malaria-endemic areas. Repeated exposure to the parasite stimulates an immune response that effectively controls infection, resulting in lower parasite densities. The age distribution influences malaria transmission. Older individuals with partial immunity experience milder infections.

Having history of malaria appeared as a significant risk factor, with participants having a 3.7-fold increased probability of infection compared to those without such a history (AOR = 3.724, 95% CI = 1.316-10.537). This finding is in agreement with the findings of former studies conducted in Cameroon (77). Previous history of malaria increases the risk of reinfection due to drug resistance in *P. falciparum* and the ability of *P. vivax* to relapse. Drug resistance can lead to incomplete parasite clearance, while *P. vivax* can reactivate from dormant liver stages, causing recurrent infections (78).

ITNs utilization was found to be a defensive factor against malaria, with 6.9 times (AOR= 6.208, 95% CI=2.380-16.191). This finding is supported by research in the Mount Cameroon area(77), in Mizan-Aman town, Ethiopia (48). This is due to the fact that ITN inhibits mosquitoes either mechanically by preventing them from entering the human body or biologically by killing insects that come into contact with it(78).

Patients who stayed out the night had a 4.5-fold higher risk of plasmodium parasite infection compared to those who did not (AOR = 4.505, 95% CI = 1.677-12.06). This finding is in line with research conducted in China-Myanmar (3).This might be due to outdoor biting by malaria-carrying mosquitoes, particularly during peak biting times at dusk and dawn. While indoor interventions like ITNs offer protection, human activities outside these hours increase exposure risk.

Malaria cases in this study were 4.1 times more common in homes near to stagnant water than in those without (AOR = 4.118, 95% CI = 1.801-9.413). This result is consistent with previous research findings from the Boset District in the East Shoa Zone of the Oromia Region of Ethiopia (76). This might be because people who live close to stagnant water are more susceptible to malaria, and stagnant water is the perfect place for malaria vectors to breed.

Travel history was also a prominent risk factor, with adults who had traveled being 3.4 times more likely to infect Plasmodium parasites as compared to those who did not (AOR = 3.365, 95% CI = 1.238-9.146). This finding is in agreement with the findings of previous studies conducted in Zambia (79), and in China (80). This suggests that movement between regions, travelers may be exposed to mosquitoes carrying plasmodium parasites in regions where the disease is prevalent, which increases the risk of infection.

This study observed significant changes in coagulation profiles due to malaria infection. PT was extended in malaria-infected patients (15.9 seconds) compared to non-infected patients (13.1 seconds), with a p-value of 0.001. INR was also elevated in malaria patients (1.27) versus non-infected individuals (1.09), significant at p = 0.001. Furthermore, APTT is extended in infected patients (37 seconds) compared to non-infected ones (29.1 seconds), with a p-value of 0.001. This was a similar finding to reports from the Demby district of the central Gondar Administrative Zone, Ethiopia (21), and also from India (81). These findings suggest disturbance of the coagulation cascade in malaria patients, which the malaria parasite can cause injury to the endothelial cells lining blood vessels. This damage can lead to the release of pro-coagulant substances, which in turn prolong PT, INR, and APTT (82).

This study revealed that significant differences in hematologic parameters exist between malaria-infected and non-infected patients. Malaria-infected individuals show higher WBC, neutrophil, eosinophil, basophil, and monocyte counts. This finding shows similar findings with a study conducted in Calabar, Nigeria (83) , Mangaluru city in southern India (84).A rise in WBC might be the body's immune response, and monocytes are essential for the immune system's reaction to malaria because they produce cytokines and deliver antigens(85).In response to malaria parasites, neutrophils produce reactive oxygen species (ROS), phagocytose, and form neutrophil extracellular traps (NETs)(86).

Malaria-infected patients show lower RBC count, HGB levels, and PLT counts compared to non-infected patients. This finding also analogous to a study conducted in Thailand-Myanmar (18). This might be due to malaria parasites causing hemolysis, destroying RBCs, which leads to decreased RBC count and HGB levels. Additionally, PLT may be sequestered in the spleen or consumed during clot formation in response to the infection (18, 87).

Furthermore, malaria-infected patients show increased MPV, PDW, and RDW. This finding is also similar to a study conducted in Thailand-Myanmar (18). In malaria-infected patients, activated platelets can enlarge, leading to increased MPV, while variability in platelet size due to different activation levels raises PDW. The malaria-induced damage to RBCs causes hemolysis and the release of cellular debris, which further stimulates platelet activation and contributes to raised MPV and PDW. Furthermore, malaria can damage bone marrow function, decreasing the production of both RBCs and PLTs. This results in a diverse red blood cell size, increasing RDW (32).

In this study measuring the diagnostic value of selected hematological profiles in predicting the severity of malaria, for differentiating malaria-positive (MP) patients from malaria-negative (MN) ones, the monocyte count exhibited the highest sensitivity at 97.6% and a strong AUC of 0.864, making it extremely effective for accurate identification. This finding was consistent with former research that was carried out in the USA (88).

RDW and PDW also demonstrated high sensitivity (97.6%) with substantial AUC values (0.775 and 0.757, respectively), indicating their strong diagnostic ability. MPV and WBC had somewhat lower sensitivities (90.2% and 87.8%, respectively) but still offered important diagnostic value with AUCs of 0.707 and 0.701. All these profiles were statistically significant ($p < 0.001$), confirming their reliability in distinguishing MP from MN patients. These diagnostic values are supported by a similar previous study conducted in India (89).

In differentiating complicated malaria (CM) from uncomplicated malaria (UM), the monocyte counts again exhibited high efficiency with a sensitivity of 88.9% and an AUC of 0.755. This finding is in line with a study conducted in Sudan (33). Overall, the study found that the monocyte count is highly effective in differentiating both MP from MN patients and also for distinguishing CM from UM. The monocyte count demonstrated strong diagnostic value, with statistically significant results supporting their effectiveness.

6. CONCLUSION

This study found a moderate malaria prevalence of 41(14.3%) in the examined population, with a prominent proportion of mild parasitemia among participants. *P. vivax* was the predominant *plasmodium* species followed by *p. falciparum*. Key factors contributing to malaria infection include having history of malaria, unable to use ITNs, closeness of house to stagnant water, having travel history, and staying night outdoor.

This study also showed that *plasmodium* infections affect the coagulation profile by elevated levels of PT, APTT, and INR in infected individuals. Besides, significant reductions in RBC count, HGB levels, and MCV, MCH, and PLT counts were observed, while monocyte, WBC, and neutrophil counts were increased.

Monocyte count, RDW, and PDW were effective in distinguishing MP patients from those without malaria. Moreover, in differentiating CM from UM cases, monocyte count obtained the best diagnostic value.

7. RECOMMENDATION

For healthcare providers, it is essential to identify key hematological markers such as monocytes, RDW, PDW, MPV, and WBC due to their diagnostic value in predicting malaria. It is essential to educate the public about malaria preventive strategies, which include using ITNs consistently, limiting nighttime outdoor exposure, removing stagnant water near homes, and taking preventative medication before visiting malaria-endemic areas.

For future research, it is advised to carry out comparable research with bigger sample sizes in order to confirm and broaden the conclusions. Additionally, longitudinal studies could provide a deeper understanding of malaria progression. Exploring the potential of molecular diagnostics, particularly PCR, could enhance the accuracy of malaria diagnosis and facilitate early detection.

8. STUDY LIMITATION

The results of this investigation might be improved since sophisticated molecular techniques, such as PCR, which have higher detection ability than light microscopy, were used for the testing.

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Structured Questionnaire

Code number ---------- Date ----------

SN	Variables	Response	
1.1	Age in full year	_____	
1.2	Please select your gender	0. Female	1. Male
1.3	Where do you currently reside?	0. Urban	1. Rural
1.4	Family Size in number	_____	
1.5	What is your education status?	0.Illiterate 1.Primary school 2. Diploma	3.Secondary 4.Degree and above
1.6	What is your occupational status?	0.Farmer 1.Daily laborer 2. Governmental	3 Merchant 4. Student
1.7	Do you have history of malaria?	0. Yes	1. No
1.8	Did you treat for malaria in the past one month?	0. Yes	1. No
1.9	Are ITNs used in your house?	0. Yes	1. No
2.0	Is IRS conducted in your home?	0.Yes	1.No
2.1	Do you stay outside at night?	0.Yes	1.No
2.2	Are there holes between the walls and roofs of your house?	0.Yes	1.No
2.3	Is there a presence of stagnant water near to your house?	0.Yes	1.No
2.4	Have you travelled outside your local area in the past one month?	0. Yes	1. No

Laboratory test results data collection sheet

Patient code_____

Laboratory tests		
Blood film microscopy	0. Negative 1. Positive	
Plasmodium species type	*0. Plasmodium vivax* *1. Plasmodium falciparum* *2.* Mixed	
Plasmodium parasite density	0. Mild (<1000 parasites/µL) 1. Moderate (1000-9999 parasites/µL) 2. Severe ((≥10,000 parasites/µL)	
Hematological profiles	WBC $x10^3$/ µL	MCV (fL)
	Neutrophil $x10^3$/ µL	MCH (pg)
	Lymphocyte $x10^3$/ µL	MCHC (g/dl)
	Monocyte $x10^3$/ µL	RDW (%)
	Eosinophil $x10^3$/ µL	PLT $x10^3$/ µL
	Basophil $x10^3$/ µL	MPV (fL)
	RBC $x10^6$/ µL	PDW (%)
	Hgb (g/dl)	
	HCT (%)	
Coagulation profiles	PT	
	INR	
	APTT	

Thank you for your participation! Your contribution is valuable for my thesis.