



**WOLKITE UNIVERSITY SCHOOL OF MEDICINE AND
HEALTH SCIENCE**

**ASSESSMENT OF MAGNITUDE OF SEVERE MALARIA CASES
AT WUSTH IN 2016E.C**

**A STUDENT RESEARCH PROJECT TO BE SUBMITTED TO THE
DEPARTMENT OF PUBLIC HEALTH, WKU, IN FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF
MEDICINE**

Prepared by: Dr. Segni Geremew (MI)

Dr Mesay Amognehegn (MI)

Dr Yalemwork Belay (MI)

Dr Befikadu Yadeta (MI)

Advisors: Dr. Shimelis Getu (Assistant professor of IM)

: Mr. Ibrahim Muktar (Assistant Professor)

DECEMBER, 2024 GC

WOLKITE, ETHIOPIA

ACKNOWLEDGMENT

First and foremost we would like to acknowledge Wolkite University College of medicine and health sciences, department of public health for giving us a chance of further education in the profession we have already engaged in.

We would like to extend our sincere thanks to our advisors Dr.Shimelis Getu (Assistant professor of Internal medicine) and Mr. Ibrahim Muktar (Assistant Professor) for their helpful guidance and encouragement, constructive suggestions throughout the research proposal and final report writing session. Your insights and expertise have been instrumental in shaping our ideas and refining our approach.

We would also like to express our gratitude WUSTH staff for providing us with all the necessary information we needed.

Contents

page No

ACKNOWLEDGMENT	I
List of Figures	II
List of Tables	III
ACRONYMS	IV
ABSTRACT	V
1. INTRODUCTION	1
1.1 Background	1
1.2 Statement of the problem	2
1.3 Significance of the study	3
2. Literature Review	3
2.1 Global burden of malaria	3
2.2 Malaria in Ethiopia	4
2.3 Etiology of malaria Disease	6
2.4 Transmission and Life cycle of malaria Parasite	6
2.5 Pathogenesis and clinical symptoms	9
2.6 Severe malaria and associated morbidity and mortality	9
3 Objective	11
3.1 General Objective	11
3.2 Specific Objectives	11
4. METHODS AND MATERIAL	11
4.1 Study area and period	11
4.2 Study design	13
4.3 Source population	13
4.4 Study population	13
4.5 Inclusion criteria	13
4.6 Exclusion criteria	13
4.7 Sample size determination and sampling technique	14
4.7.1 Sample size	14

4.7.2 Sampling technique	14
4.7.3 Data collection procedure and Pretest.....	15
4.8 Study variables	15
4.8.1 Dependent variable	15
4.8.2 Independent variable.....	15
4.9 Operational definition.....	15
4.10 Data Quality Assurance.....	16
4.11 Ethical consideration.....	16
4.12 Data Processing and Analysis.....	17
4.13. Dissemination of the result plan.....	17
5.RESULTS	17
5.1 Socio demographic Characteristics	17
5.2 Presenting symptoms and Duration of symptoms prior to hospital visit.....	18
5.3 Malaria and other diagnosis	20
5.4 Methods of Malarial diagnosis and Type of parasite identified	20
5.5 Diagnosis of severe malaria and severity features	22
5.6 Seasonality and previous malarial attack	23
5.7 Treatment of malarial patients	24
5.8 Duration of hospital stay and Treatment Outcome	25
5.9 Factors Associated with severe malaria.....	26
6.DISCUSSION	28
7.Strength and weakness of the study.....	31
7.1 Strength of the study	32
7.2 Limitation of the study.....	32
8.CONCLUSIONS AND RECOMMENDATIONS	32
8.1 Conclusion.....	32
8.2 Recommendation.....	32
REFERENCES	33
Annex	35

List of Figures

Figure-2.1 Life cycle of Plasmodium species.

Figure-3.1 Map of the study area.

Figure 5.1 Type of parasite identified in malarial patient visited WKUSTH in 2016E.C

Figure 5.2 Diagnosis of severe malaria

Figure 5.3 Treatment Outcome of severe malaria patients who was treated at WKUSTH in 2016E.C

List of Tables

Table 5.1 Socio demographic characteristics of malaria and severe malaria patient who visited and treated at WKUSTH in 2016E.C.

Table 5.2 Presenting symptom and duration of symptom prior to hospital visit of patients who visited and treated at WKUSTH in 2016E.C

Table 5.3 Malaria and other diagnosis of patients that visited WKUSTH in 2016E.C

Table 5.4 Method of malarial diagnosis and type of parasite identified in patient visited WKUSTH in 2016E.C

Table 5.5 Diagnosis of severe malaria and severity features

Table 5.6 seasonality, history of previous malarial attack and comorbidity

Table 5.7 Treatment of malarial patients at WKUSTH in 2016

Table 5.8 duration of hospital stay of malaria and S malaria patient

Table 5.9 Treatment Outcome of patient who was treated at WKUSTH in 2016

Table 5.10: Bi variate and multivariate analysis of factors associated with magnitude of severe malaria in WUSTH IN 2016

ACRONYMS

ACT - Artemisinin-based combination Therapy

CDC - Centre for Disease Control and Prevention

CFR - Case Fatality Rate

CQ - Chloroquine

EDHS - Ethiopia Demographic and Health Survey

FMOH - Federal Ministry of Health

HEWs - Health Extension worker

HSDP -Health Sector Development Program

IRS - Indoor-Residual spraying

ITNs - Insecticide Treated Net

LLIN - Long Lasting Insecticidal Nets

MIS - malaria Indicator Survey

MOH- Ministry of Health

MOP - Malaria Operational Plan

MOSHE -Ministry of Science and Higher Education

PCR- Polymerase chain Reaction

RDT - Rapid Diagnostic Test

SNNPRs -Southern Nation, Nationalities and Regional States

SPSS - Statistical Package for Social science

UNESCO -United Nations Educational, Scientific and cultural Organization

USAID United States Agency

WHO - World health organization

WKU- Wolkite University

WUSH –Wolkite university specialized hospital

ABSTRACT

Background -In Ethiopia, Malaria burden have been reduced over the last two decades due to improved coverage of key malaria interventions through-out the country (FDREMH report, 2015 and Tafesse et al, 2018). Even though these gains, in the previous years, Malaria still remains the leading cause of outpatient visits, health facility admissions and inpatient deaths (FMOH, 2012). In 2016, there were an estimated 2,927,266 new malaria cases and 4782 deaths (Girum et al, 2016)..

Objectives: The main objective of the study was Facility-based retrospective cross sectional study of severe malaria cases in wolkite university specialized hospital, Gurage zone, Central Ethiopia, 2016 E.C.

Methodology: A retrospective documentary review study will be conducted at an institution to evaluate magnitude of severe malaria cases among patients admitted at WUSH in 2016 E.C. A sample size of 403 was taken by using systematic sampling method from patients who visited WUSTH. The data was analyzed using SPSS software version 27 and presented by tables, graphs and charts. Descriptive statistics and binary logistic regression was employed, and the degree of association was calculated using odds ratios with 95% CI. A p-value of less than 0.05 was considered significant for associations between dependent and independent variables

Result: A total of 403 patients were involved in this study among the participants 11%(44) were <18 years, 81.6%(329) were 18 to 65 years. Among patient who were enrolled in this study, more than half of them 214(53.1%) were male. Highest proportion of patients in the survey 257 (63.8%) live in rural area. From our study the most common presenting symptom of patient were cough and shortness of breath 21.8%(88), abdominal pain 17.6%(71), symptom of malaria (Fever, headache, chills, nausea, vomiting) 14.6%(59). Most of the patient visited the hospital after 3 days of experiencing symptoms 60.5%(244) as well as Most of malarial and severe malarial patients visited hospital after 3 days of experiencing symptoms. Out of 403

patients malaria accounts for 16.9%(68).Other common diagnosed diseases were Pneumonia 15.6%(63) ,Dyspepsia 12.4%(50) and CHF 8.4%(34).Most of Malarial cases were diagnosed microscopically 83.8%(57) and the remaining were diagnosed clinically by sign and symptom .Plasmodium falciparum account for most malarial diseases 47.1%(32) and plasmodium vivax was the next etiology responsible for it.Almost all cases of severe malaria 95%(19) were caused by Plasmodium falciparum .From our study those who was diagnosed with malaria(68) 29.4%(20) had severe malaria.The common severity features of severe malaria seen were severe anemia 40%(8),Prostration 25%(5),cerebral malaria 15%(3) and Hypoglycemia 15%(3).Most of malarial cases occur in autumn 57.4%(39) especially in September and October and spring season 23.5%(16)From those who had S.malaria about 70%(14) had previous history of malarial attack .From those who had S.malaria 15%(3) had comorbidity.5%(7) S.malaria patients had more than 3 days hospital stay.From patients diagnosed with severe malaria 20%(4) were died and 80%(16) fully recovered compared to other diagnosis that had 0.3% mortality rate

Conclusion:Although prevalence of malaria seems decreasing due to intensive intervention and combined strategies approaches in the country, clinical data showed that, malaria is still a major health problem in the study area. Both P. falciparum and P. vivax were reported. Overall, P. falciparum was 47.1% followed by p.vivax 27.9% and mixed-infection cases 8.8% .Males were more affected than females. The highest malaria prevalence in age b/n 15 -45 yrs. The distribution of malaria showed seasonality with the highest prevalence in autumn followed by spring season. Severe malaria complications associated such as prostration, severe anemia, Cerebral malaria and hypoglycemia were observed in the study area. Regarding treatment outcome of Severe malaria 20% (4/20) was died the remaining 80% (16) are recovered and discharged.

1. INTRODUCTION

1.1 Background

Malaria is an infectious disease that has a major impact on global public health and the economy, with an estimated 3.4 billion people at risk. Currently, malaria threatens almost one third of the world's population in 104 tropical countries and territories where it is considered an endemic disease. The World Health Organization (WHO) estimates that 249 million cases of malaria occurred globally in 2022 and led to 608,000 deaths. Africa, South-East Asia and the Eastern Mediterranean were the regions with the highest numbers of reported cases and deaths reported, mainly in children under five years of age. Malaria is caused by a protozoan belonging to the genus, Plasmodium, which are obligate intracellular protozoa. *P. falciparum* (60%) and *P. vivax* (40%) are the two key causes of malaria. *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi* infect humans and *P. falciparum* is the most highly virulent.

Mosquitoes of the *Anopheles* genus are the vectors of the *Plasmodium* species, the causative agents of malarial disease. More than 400 species of the *Anopheles* mosquito have been described and approximately 70 of these species are potential vectors of malaria that affect humans (Sinka et al. 2012).

The most predominant and widely distributed parasites in Ethiopia are *P. falciparum* and *P. vivax*, constituting 60% and 40% of malaria cases, respectively (FMOH, 2012). Around 68% of Ethiopian landmass is considered endemic for malaria, putting 60% of the total population more at risk of contracting the disease (EPHIENMIS, 2016). The transmission intensity and levels of malaria risk show marked seasonal, inter-annual and spatial variability; with the exception of the southwestern low land area where transmission is year-around (Zhou et al., 2016). Malaria transmission becomes high from September to December following the heavy summer rainy season and lower transmission lasts from April to May following the short rainy season in most regions of Ethiopia. Also, prevalence and incidence of malaria vary

depending on variations in socio-demographic risk factors, including age and sex. The unstable transmission patterns along with environmental modifications often make the country prone to cyclic epidemics occurring every 5 to 8 years (FDREMH report, 2015, EPHIENMIS, 2016). For this reason, to monitor and measure the impact of interventions, monitoring malaria burden and trend in endemic areas is critical. However, such useful data remain scarce in several endemic areas of Ethiopia, particularly in parts of SNNP Regional State.

1.2 Statement of the problem

According to World Malaria Report (2022) malaria is among the most frequently occurring and distracting phenomenon that affects an average 26,400,000 (27% of total population) reside in malaria high transmission areas (>1 confirmed cases per 1000 population), 39,600,000 (41%) in low (1 case per 1000 population) and 31,000,000 (32%) malaria free (0 cases per 1000 population) in 2014. Children, particularly under -five, including newborns and infants less than 12 months of age are one of the most exposed groups affected by malaria bearing 69 % of the above deaths point out that in high malaria transmission areas, infants become vulnerable to malaria at approximately 3 months of age. When immunity acquired from the mother starts to go down and are becoming at increased risk of rapid disease progression, severe malaria and death, severe anemia, hypoglycemia and cerebral malaria are features of severe malaria which are particularly common in this age group (WHO, 2016).

A large peak in malaria case occurs during the major transmission season from September to December, following the main rains June to August. The second transmission seasons in April and May following short rains are a second but less pronounced peak occurs. Due to this unstable and seasonal transmission pattern of malaria in the country, protective immunity of not only children but the general population is low and all age groups are highly vulnerable to the disease. Thus the public health burden of malaria is huge in Ethiopia (FMoH, 2015).

There were no studies conducted on the problem so as to investigate the prevalence of malaria in WUSTH catchment area. Therefore, this study focuses on the retrospective assessment of malaria in WUSTH for the last year (2016). This study was, therefore, designed with the following significance.

1.3 Significance of the study

It is obvious that the global malaria status is the sum total of each country status, and in turn the country status is the sum total of its regional and local situations at each level. Accurate assessments of the levels and time trends in malaria burden are crucial for the assessment of progress towards goals and planning national health services and also the study may be used as baseline information for future study or intervention and encourage researchers to give emphasis to the prevention and control program of malaria focusing future efforts (R.E.Cibulskis et al., 2009)

Despite the aforementioned studies at different parts of the country, malaria situation with regard to its trend, seasonal patterns, and distribution, remains unknown in the study area. Therefore, this study was aimed at determining the trend of malaria occurrence in the WUSTH over the last year 2016 (E.C).

The study provides scientific evidence that would be an important data base of local, national, and global relevance in advancing current knowledge on malaria situation. It is also useful to policy makers and program planners at each level for assessing progress and focusing future efforts while providing evidence-driven public health action in preventing and controlling malaria incidence.

2. Literature Review

2.1 Global burden of malaria

Malaria is a major public health problem that still results in illness and death. Globally, malaria cases increased from 227 million cases in 2019 to 241 million in 2020, reported 85 malaria endemic countries. In the last two years, global malaria case numbers have risen by 14million case and deaths by 47,000 due to disruption during the Covid pandemic. Malaria is one of the

major diseases affecting people of low socioeconomic in developing countries. The majority of the global malarial burden is in sub-Saharan Africa, with the highest global case and death that can be observed from these regions, which accounted for the majority (95%) of these cases. Nigeria (27%), the Democratic Republic of Congo (12%), Uganda (5%) , Mozambique(4%), Niger(3%), accounted about 51% of all cases globally. It hurts people's health as well as the economic development many developing countries.(1,4,5)

In the world there are an estimated 3.3 billion people are at risk of being infected with malaria and developing disease, and 1.2 billion are at high risk to acquire the disease. The burden is heaviest in the WHO African Region, where an estimated 90% of all malaria deaths occur, and in children aged less than 5 years, which account for 78% of all deaths (WHO, 2014). It estimated 660,000deaths in 2011 directly attributed to malaria, approximately half of the world s population being at risk of infection. The disease remains one of the major challenges for people's health and livelihood around the world (WHO, 2015). Nearly half of the world s population is living under the risk of malaria. As per the WHO estimates, 91 countries and territories had an ongoing transmission of malaria in 2015 with 212 million identified cases and 429,000 deaths. Most number of cases was reported from the African Region, followed by the Southeast Asia Region (WHO, 2016). WHO recently launched the GTS for malaria, which aims to reduce the incidence and mortality rates of malaria at least by 90% by 2030.

2.2 Malaria in Ethiopia

Malaria morbidity and mortality have been significantly decreased in Ethiopia in the past decade. Ethiopia's fight against malaria started many years ago and transmission of this infectious disease significantly decreased since 1959. However, malaria still remains a major public health problem in Ethiopia. Ethiopia has a population of more than 100 million, and it is estimated that ~ 68% of the population is at risk of the disease. Plasmodium falciparum and P. vivax co-exist as major parasite species in Ethiopia (WHO, 2017). This epidemiologic feature makes malaria control more complicated than in most African countries where P. vivax has low or nil endemicity. Malaria transmission in Ethiopia occurs mainly at altitudes < 2000 m, although endemic regions > 2000 m have been reported (FMoH, 2010). The levels of malaria risk and transmission intensity, however, show marked seasonal, inter-annual and spatial variability, with the exception of the southwestern international border low land area where transmission is year-around (Zhou et al., 2016). In most regions of the country, the major

transmission season is from September to December, following the main rainy season from June to September. There is a short transmission season from April to May following the short rainy season in some regions. (WHO,2023)

Anopheles arabiensis is the predominant vector with *An. pharoensis*, *An. coustani*, *An. funestus* and *An. nili* having a minor role in transmission. Generally, the diverse ecology of the country supports a wide range of transmission intensities ranging from low-seasonal to high-perennial transmission. For planning purposes and targeting of intervention strategies, the Federal Ministry of Health (FMOH) of Ethiopia has stratified the country's malaria transmission burden using 'woreda' (district)-level transmission intensity according to annual parasite incidence per 1000 population (API) and elevation. Accordingly, four broad strata were identified by the mixed criteria of the FMOH and World Health Organization (WHO) malaria free, low, moderate, and high transmission. *Plasmodium falciparum* are endemic in many regions of the country. *Plasmodium malariae* and *P. ovale* infection are uncommon and account for < 1% of confirmed malaria cases (FMOH, 2010). In the past decade Ethiopia has made significant strides in expanding coverage of key malaria interventions throughout the country. Indoor residual spraying (IRS) using dichlorodi-phenyltrichloroethane (DDT) was introduced in 1959 with the global malaria eradication campaign, and since then different chemical insecticides have been used for malaria control (AIRS, 2016). Insecticide treated nets (ITN) were introduced in 1997 as an additional intervention. Chloroquine was the first line treatment of all malaria species in Ethiopia before 1998. It was replaced by sulfa doxine-pyrimethamine (SP) after 1998 for the treatment of uncomplicated *P. falciparum* due to widespread decline in the efficacy of CQ. Parasites soon developed resistance to SP drugs.

Planning for scaling-up malaria prevention and control interventions started in 2003 with the support from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) (Kassa et al.,2005). In 2004, the FMOH introduced artemisinin-based combination therapy (ACT) as the first-line drug for treatment of *P.falciparum* malaria as well as rapid diagnostic tests (RDT) to improve diagnosis and long-lasting insecticidal nets (LLINs) as a method of preventing transmission of parasite from mosquitoes to people. Major scale-up began in 2005 with countrywide distribution of RDTs, ACTs, LLINs and implementation of IRS.

2.3 Etiology of malaria Disease

A protozoan parasite belonging to the Genus Plasmodium causes malaria with five species: *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi* infect humans (Snow, 2005) and is transmitted to humans through a bite from one of 40 species of female *An. mosquitoes*.

Plasmodium is transmitted by mosquitoes. Female mosquitoes belonging to the genus *An.* are responsible for plasmodium transmission. Of over 430 *An.* species, only 30-40 transmit malaria in nature and *Anopheles gambiae* complex is the most prominent plasmodium vector in Africa.

The mosquitoes which act as vector for this disease are female *An. funestus*, *An. moucheti*, *An. gambiae*, *An. arabiensis* (Karl et al., 2014; WHO, 2015). *Plasmodium falciparum* is responsible for almost all of the 1.7–2.5 million deaths worldwide caused by malaria and *P.*

falciparum remains the single most important threat to public health at a global scale, accounting for more than 90% of the world's malaria mortality. A fifth *Plasmodium* species named *P.*

knowlesi, that previously was known to only infect macaques, has also newly been shown to be able to infect humans (Baird, 2013). Africa had no malaria before and according to Nandi elders, malaria was introduced into Africa by African soldiers who participated in First World War in 1918 and 1919 and after coming back, 25% of the indigenous population got the disease

(Lindsay and Martens, 1998). The relationship between humans and malaria may date back several million years (Escalante et al., 1998). Among several *Plasmodium* species that cause

human malaria naturally *P. falciparum* is by far the most severe and widespread. *P. vivax* malaria, traditionally observed as a relatively benign form of the disease, is the next dominant species and can also be a major cause of morbidity and mortality, in infants and young children.

A recent study from India reported *P. vivax* as a cause of acute respiratory distress syndrome which is commonly associated to *P. falciparum*. *P. ovale* and *P. malariae* are relatively rare and are usually not life-threatening (Cox-Singh, 2008).

2.4 Transmission and Life cycle of malaria Parasite

Malaria infection may be acquired congenitally from mother to baby across the placenta, from platelet or blood transfusions and from the use of shared needles; however it is most frequently initiated with the bite of an infected, female *Anopheles* mosquito, which injects the sporozoite stage of the parasite with its bite (Moriya et al., 2009). The malaria parasite life cycle involves two hosts (Figure 2.1). During a blood meal, a malaria infected female *Anopheles* mosquito inoculates sporozoites into the human host. After sporozoites or the infective stages, are injected

they make quick work of invading liver cells (hepatocytes) using the apical organelles (Garnham, 1988). In most cases, relatively few sporozoites are injected (approximately 8-15), but up to 100 may be introduced in some instances, after injection, they enter the circulation, either directly or via lymph channels (approximately 20%), and rapidly target the hepatic parenchyma cells (Garnham, 1988). Within 45 min of the bite, all sporozoites have either entered the hepatocytes or have been cleared. Each sporozoite bores into the hepatocyte and there begins a phase of asexual reproduction. This stage lasts on average between 5.5 for *P. falciparum* and 15 days for *P. malariae* before the hepatic schizont ruptures to release merozoites into the blood stream (Garnham, 1988; Moriya et al., 2009)

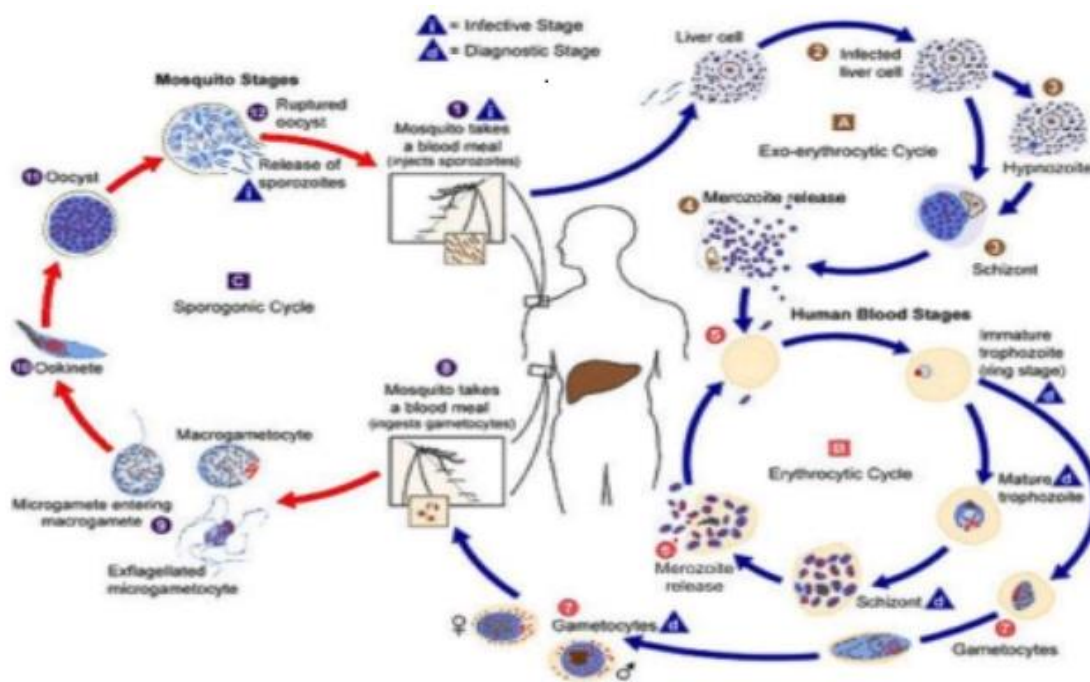


Fig. 2.1 Life cycle of Plasmodium species.

Source: CDC [http:// www.dpd.cdc.gov/dpdx/HTML/Malaria.htm](http://www.dpd.cdc.gov/dpdx/HTML/Malaria.htm).

The infective stages, which are injected by a mosquito are carried around the body until they invade liver hepatocytes where they undergo a phase of asexual multiplication (exoerythrocytic schizogony) resulting in the production of many uninucleate merozoites (Bannister et al., 2001). At the end of the hepatic stage of development, a single sporozoite can develop into a schizont that contains thousands of daughter parasites that fill the hepatocyte. Infected hepatocytes burst and release numerous merozoites into the bloodstream. *P. falciparum* can complete this liver

stage within 7 days and each of its sporozoites produces about 40,000 daughter parasites (Moriya et al., 2009).

For *P. vivax*, these values are 6-8 days and 10,000 merozoites; for *P. malariae*, 12-16 days and 2000 merozoites; and for *P. ovale*, 9 days and 15,000 merozoites. In the case of *P. vivax* and *P. ovale*, some sporozoites transform to the dormant hypnozoite, remaining viable for up to 50 years (Bannister et al., 2001). This stage is responsible for relapses when it re-enters its developmental cycle. Inside the host's liver cell it undergoes asexual replication. Next stage of development, called the erythrocytic or blood stage, is initiated when exo-erythrocytic merozoites from the liver invade red blood cells (RBCs) (James et al., 2004).

Merozoites of *P. falciparum* can infect RBCs of all ages, whereas those of *P. vivax* and *P. ovale* infect reticulocytes and those of *P. malariae* invade only older RBCs (James et al., 2004; Moriya et al., 2009). Shortly after merozoites are released from hepatocytes, they invade RBCs and over a period of 2 or 3 days, develop asexually. The time from invasion to exit varies with species, 48 hrs for *P. falciparum* and *P. vivax* and 72 h for *P. malariae* and *P. ovale*, the synchronous release of merozoites coinciding with fever peaks (Bannister et al., 2009). The stages of asexual development include the ring (early trophozoite), trophozoite and schizont stages (James et al., 2004; Moriya et al., 2009).

At maturation, the schizont bursts and releases merozoites into the blood circulation. Most of the released merozoites re-invade a new erythrocyte, thereby repeating their asexual life cycle (blood stage cycle). In some instances, however, invasion of an erythrocyte by a merozoite initiates sexual development instead of asexual development (James et al., 2004; Moriya et al., 2009). Thus, merozoites may develop into male gametocytes (microgametocytes) or female gametocytes (macro gametocytes). These gametocytes can develop further only when they are taken up by an appropriate species of *Anopheles* mosquito during a blood meal. They subsequently mate within the gut of the mosquito, the definitive host (Cox, 2010). The parasites eventually become sporozoites, which reach the salivary gland of the mosquito. With the next bite, the infected mosquito releases sporozoites into the host, thereby completing the life cycle (Bannister et al., 2001).

2.5 Pathogenesis and clinical symptoms

Severe and life-threatening complications mainly due to *P.falciparum* sometimes *P. vivax* may be due to the change in the clinical spectrum of disease, increase in resistance, indiscriminate use of anti-malarial drugs, delayed treatment (Alexandre *et al.*, 2010; Kute *et al.*, 2011; Kumar and Ghildiyal, 2014).

All age groups suffer *P.falciparum* infections and endure repeated, incapacitating febrile attacks, and develop clinical complications, such as jaundice, shock, severe anemia, respiratory distress, cerebral malaria, dysfunction of different organs, hypoglycemia, thrombocytopenia, hepatic dysfunction, acute kidney injury and hypotension with poor outcomes in pregnancy and learning impairment in children (Alexandre *et al.*, 2010; Lacerda *et al.*, 2012; Ric *et al.*, 2014; Dasgupta *et al.*, 2015).

Malaria in pregnancy is associated with increased risks of maternal anemia, hypoglycaemia, ARDS, spontaneous abortion, premature delivery and other adverse effects on health, placental parasitaemia is associated with low birth-weight infants, the risk of severe disease extends into the immediate postpartum period (WHO, 2000).

Key features of malaria are the adherence of infected red blood cells to the endothelium of small blood vessels compromising blood flow through tissues, and the production of pro-inflammatory cytokines (Parise and Lewis, 2005). Factors that determine whether a patient develops mild or severe disease are complex and multi-factorial and are related to both the parasite and the host. Parasites causing severe malaria have a greater multiplication potential than those causing uncomplicated infections (Parise and Lewis, 2005)

2.6 Severe malaria and associated morbidity and mortality

Severe malaria by definition is associated with a high mortality, from a clinical perspective; there is a continuum from asymptomatic malaria to uncomplicated illness through to severe and lethal malaria (Murray *et al.*, 2012).

Almost all severe forms and deaths from malaria are caused by *P.falciparum*. With an implementation of molecular diagnosis, it has become evident that *P. vivax* mono infection could also result in multiorgan dysfunction as well as severe life threatening and fatal disease both in

adults and in children as seen in *P. falciparum* infection (Anstey et al. 2012; Patil et al., 2015). It was previously presumed that the severe disease with vivax infection is actually caused by co-infection of vivax and falciparum species (Picot, 2006; Murray et al., 2012). However with application of the recently developed tests of malarial antigen and the nucleic acid amplification technique it has become evident that vivax mono infection can be a cause of severe malaria and death. PCR test which is used mainly for the academic purpose can also differentiate between vivax mono-infection and falciparum infection (Picot, 2006; Murray et al., 2012). In 1990, the World Health Organization (WHO) established criteria for severe malaria in order to assist future clinical and epidemiological studies (WHO, 1990). In 2000, the WHO revised these criteria to include other clinical manifestations and laboratory values that portend a poor prognosis based on clinical experience in semi-immune patients (WHO, 2000). The major complications of severe malaria can develop rapidly and progress to death within hours or days (WHO, 2000). There are many risk factors that are related to severe malaria and death include age greater than 65 years, female sex (especially when associated with pregnancy), pediatric patients especially children under 5 years, non-immune status, coexisting medical conditions, no anti-malarial prophylaxis, delay in treatment, and severity of the illness at admission (Rodriguez-Morales et al., 2015)

2.7. Challenge towards elimination Malaria

As Carlton et al. (2011) noted *P. vivax* malaria control program require early diagnosis combined with highly efficacious treatment to cure dormant liver and blood-stage parasites. In addition, disruption of mosquito bite transmission is key, preferably through sustainable community-based vector control programs and routine use of drugs that target the mosquito transmission ('gametocyte') stages found in human blood. However, case detection is inherently more challenging for *P. vivax* malaria due to two of its biological properties (Carlton et al., 2011). First, the parasite's strong preference to infect the minor population of reticulocytes (immature red blood cells) in the bloodstream results in significantly lower parasitemia (WHO, 2014). In many endemic regions *P. vivax* is often overlooked in co-infections with *P. falciparum*, and newly available rapid diagnostic tests have sub-optimal sensitivity for *P. vivax* (Carlton et al., 2011). Carlton et al. (2011) explained the second and more significant problem stems from

invisible dormant liver stages that can give rise to multiple periodic ‘relapse infections’ up to several years after an infectious mosquito bite (Carlton et al., 2011). The unpredictable nature of relapse infections, which can vary from as short as three weeks for tropical strains to five years for strains circulating in temperate climates, further complicates elimination programs since gametocytes typically appear at the earliest onset of clinical symptoms, allowing transmission of *P. vivax* before treatment can be initiated (Battle et al., 2014, White, 2008). *P. vivax* control may become even more difficult in coming years as there is increasing prevalence of clinically defined chloroquine-resistant *P. vivax*, for which little monitoring is possible without in vitro culture or a genetic marker for resistance (Price et al., 2009; Carlton et al., 2011)

3 Objective

3.1 General Objective

The general objective of the study was Facility-based retrospective cross sectional study of severe malaria cases admitted at Wolkite university specialized hospital, Gurage zone, Central Ethiopia, 2016 E.C.

3.2 Specific Objectives

- To determine the magnitude and pattern of severe malaria among patients admitted at Wolkite University specialized hospital in 2016 E.C.
- To identify factors that are associated with severe malaria among patients admitted at Wolkite University specialized hospital in 2016 E.C.

4. METHODS AND MATERIAL

4.1 Study area and period

The study was conducted at Wolkite university specialized teaching Hospital (WUSTH). It is a referral hospital located in Gubre sub-city, Gurage zone, Central Ethiopia.

Gubre sub city is located at about 12 km away from Wolkite town in Southwest direction.

Wolkite town is the capital city of Gurage zone 158 km away from Southwest of Addis Ababa.

The geographical location of the town is approximately 8° 17' N latitude and 37° 47' E longitude.

The average elevation of the town is about 1855 m above sea level. The mean annual temperature of the zone ranges between 13-30°C with annual average temperature of 32°C.

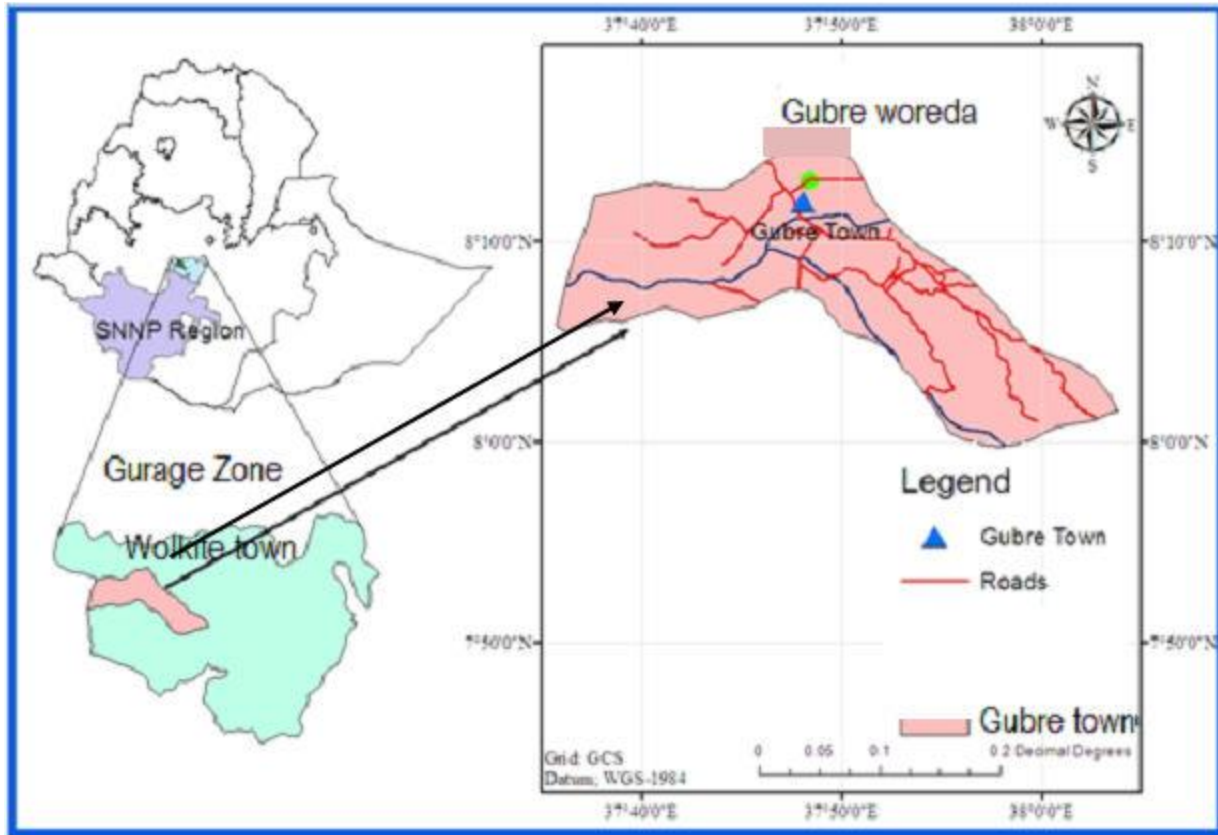


Figure-3.1 Map of the study area.

The town has weynadega climatic condition with the mean annual rain fall ranges 600-1600 mm. According to the statistics obtained from Wolkite’s Town Municipality, the population was 70,796 out of which 35, 848 were males and 34,948 females. The population is multi-ethnic, the Gurage constituting the majority.

Wolkite university specialized teaching hospital (WUSTH) was established on Hamile 29 2011 EC. This hospital provided full health care service for population of Gurage zone and its surrounding in Oromia region such as silk amba and keta wayu as their primary catchment areas. The total number of staff of the hospital was 406 including 11 surgeon, 5 gynecologist-obstetrician, 9 internist, 8 pediatricians, 59 residents, 23 general practitioners, 10 health officers,

9 anesthetists, 1 dentist, 2 psychiatrist, 2 ophthalmologist, 2 radiologist, 1 pathologist, 128 nurses, 25 laboratory technologists, and 24 pharmacists.

The study was conducted from September 1, 2016 E.C to Puagume 5, 2016 E.C.

4.2 Study design

A Hospital based Retrospective cross-sectional study was conducted at WUSH in 2016 E.C

4.3 Source population

All patients that visited and treated at Wolkite university specialized teaching Hospital in 2016 E.C.

4.4 Study population

All patients that were randomly selected from those who visited WKUSH in 2016 E.C

4.5 Inclusion criteria

All patient that were treated at:

- ◆ Medical OPD, Emergency & ward;
- ◆ Pediatrics OPD, Emergency & ward;
- ◆ Gyn Emergency and ANC during study period

4.6 Exclusion criteria

- ◆ All Patients who had incomplete medical record (the exclusion criteria will be if >5 of questions are not answered)
- ◆ All neonates admitted at age equal to or less than 28 days to the NICU of WUSH during study period
- ◆ All Pregnant mothers who were admitted to Labor ward during study period.

- ◆ All patients who were treated at: Surgery OPD, Emergency & ward; GynOPD; Psychiatry OPD and Ward; Ophthalmology OPD and Ward; Dermatology OPD during study period

4.7 Sample size determination and sampling technique

4.7.1 Sample size

Sample size was determined by the number of patients admitted during the time period from September 1, 2016 E.C to 5/13/16 E.C. Sample size was calculated using single population proportion sample size calculation formula by assuming 50% of case fatality to yield the maximum representative sample size with 95% confidence interval.

$$n = (Z\alpha/2)^2 * p (1-p)/d^2$$

Where:-

n= required sample size

z= critical value at 95% CI (1.96)

p= prevalence rate since the magnitude of mortality is not known, p is taken as 50% i.e 0.5

Margin of error (d) to be 5% (d = 0.05)

$$n = \frac{(1.96)^2 * 0.5(1-0.5)}{(0.05)^2} \quad n = 384$$

Adding 5% for incomplete medical record to 384 = **403**

Therefore a total of **403** samples were used to conduct this study

4.7.2 Sampling technique

In the study population, there were 26,500 patients who visited WUSH in 2016 E.C. The sampling technique used was the systematic random sampling. The sampling interval was determined by the formula $N/n = 66$ and after the calculation it became 1 in every 66 charts, so one every patient medical record was taken from the HMIS log book by the next card for those

cards which fulfill exclusion criteria and then continues every 66th Value in similar pattern until the required numbers of samples were collected.

4.7.3 Data collection procedure and Pretest

The questionnaire had five parts which includes: Socio-demographic characteristics; Clinical history, Diagnosis and lab methods, Treatment & outcome and other. Records of Selected patients for the last one year (2016 E.C) were reviewed. This involved going through the HMIS Log book records of patient from 1/1/16 E.c to 5/13/16 E.C The diagnosis was identified from medical files of patients. The medical charts were traced using the patient card numbers on the log book registry.

4.8 Study variables

4.8.1 Dependent variable

Magnitude of severe malaria

4.8.2 Independent variable

- Socio-Demographic factors: Age, Sex, place of residence
- Severity features: Impaired consciousness, Severe anemia, Renal impairment, Pulmonary oedema, Jaundice, Shock, Acidosis, Seizure, Hypoglycemia
- Anti-malaria drug type
- Other factors: Hospital stay, Time before admission, Type of plasmodium species

4.9 Operational definition

Severe Malaria- is characterized by one of the following features: Impaired consciousness , Prostration , Severe anemia , Jaundice, Hypoglycemia, Abnormal bleeding

Prostration- is inability to sit, stand, or eat without support, in the absence of impaired

consciousness.

Cerebral malaria- is the presence of coma(loss of consciousness) with *P. falciparum* parasitemia and an absence of other reasons for coma.

Sever anemia-is hemoglobin level <5 g/dL or Hct <15%

Hypoglycemia-blood glucose level <40mg/dl

Comorbidity- is medical conditions that coexist alongside primary diagnosis

Antipyretic is drugs that reduce fever

Recovered -is to regain a normal or healthy state or cured

Autumn-september,October,November

Spring-March,April, May

Summer-June,July,August

Winter-December,January,february

Urban-towns or cities

Rural -is a regions outside of cities and towns

4.10 Data Quality Assurance

The quality of data was controlled starting from the time of questionnaires preparations. The collected data was manually checked for completeness, accuracy and clarity by the data collectors,then it was transferred to SPSS version 27 for analysis. Each chart was given a case number to avoid mixing and for confidentiality.

4.11 Ethical consideration

First a permission letter to conduct the study was obtained from Wolkite university CMHS department of public health. Permission from medical director was taken then the objective of the study was briefed to the staff of the documentation department.Documents were kept confidential.

4.12 Data Processing and Analysis

After the data collection was completed, the data was entered to SPSS version 27. Descriptive statistics and binary logistic regression was employed, and the degree of association was calculated using odds ratios with 95% confidence intervals. A p-value of less than 0.05 was considered significant for associations between dependent and independent variables. Binary and multivariate logistic regression was done to see the effect of each of the independent variables on the outcome variable by simultaneously suppressing the effect of extraneous variables. A descriptive statistic was performed to determine frequency, proportion and percentage. The data presentation will be presented by table, figures, chart, and bar graph.

4.13. Dissemination of the result plan

The final result of this paper will be submitted to Wolkite University College of medicine and health science, department of public health. The finding of this study will be disseminated through presentation and publication.

5.RESULTS

5.1 Socio demographic Characteristics

A total of 403 patients were involved in this study with a response rate of 100%

Among the participants 11%(44) were <18years,81.6%(329) were between 18 to 65 years

Among patient who were enrolled in this study, more than half of them 214(53.1%) were male.

Highest proportion of patients in the survey 257 (63.8%) live in rural area. Highest proportion of S. malaria patients were male75%(15) and 95% (19) live in rural.

characteristics		frequency		Percentage	
		Malaria	S malaria	Malaria	S.malaria
Sex	Male	41	15	60.3%	75%
	Female	27	5	39.7%	25%
Age	0-14	2	2	2.9%	10%
	15-30	25	9	36.8%	45%
	31-45	37	9	54.4%	45%
	>46	4	-	5.9%	-
Residency	Urban	35	19	51.5%	95%
	Rural	33	1	48.5%	5.0%

Table 5.1 Socio-demographic characteristics of malaria and sever malaria patient who visited and treated at WKUSTH in 2016 E.C

5.2 Presenting symptoms and Duration of symptoms prior to hospital visit

From our study the most common presenting symptom of patient were cough and shortness of breath 21.8%(88),abdominal pain 17.6%(71),symptom of malaria(Fever,headache,chills,nausea,vomiting) 14.6%(59)

Most of the patient visited the hospital after 3 days of experiencing symptoms 60.5%(244) as well as Most of malarial and severe malarial patients visited hospital after 3 days of experiencing symptoms.

Variables	Presenting symptoms	Frequency		Percentage	
Symptoms	Cough and shortness of breath	88		21.8%	
	abdominal pain	71		17.6%	
	Fever, headache,chills, nausea,vomiting	59		14.6%	
	Loss of consciousness,abnormal body movement	50		12.4%	
	GBS	43		10.7%	
	Fatigue,vertigo,tinnitus	35		8.7%	
	Others	57		14.1%	
Duration of symptom prior to hospital visit		Malaria	S.malaria	Malaria	S.malaria
	With in a day	8	1	11.8%	5%
	1 to 3 days	47	14	19.1%	25%
	After 3 days	13	5	69.1%	70%

Table 5.2 Presenting symptom and duration of symptom prior to hospital visit of patients who visited and treated at WKUSTH in 2016

5.3 Malaria and other diagnosis

Out of 403 patients malaria accounts for 16.9%(68).Other common diagnosed diseases were Pneumonia 15.6%(63),Dyspepsia 12.4%(50) and CHF8.4%(34).

Variables		Frequency	Percentage
Malaria		68	16.9%
Other diagnosis	CAP	63	15.6%
	Dyspepsia	50	12.4%
	CHF	34	8.4%
	HTN	31	7.7%
	PNP	25	6.2%
	DM	22	5.5%
	Sepsis	22	5.5%
	Other	88	21.8%

Table 5.3 Malaria and other diagnosis of patients that visited WKUSTH in 2016E.C

5.4 Methods of Malarial diagnosis and Type of parasite identified

Most of Malarial cases were diagnosed microscopically 83.8%(57) and the remaining were diagnosed clinically by sign and symptom .Plasmodium falciparum account for most malarial diseases 47.1%(32) and plasmodium vivax was the next etiology responsible for it.Almost all cases of severe malaria 95%(19) were caused by Plasmodium falciparum .

Variables		Frequency	Percentage
Method of malarial diagnosis	Microscopy	57	83.8%
	clinically	11	16.2%
Type of malarial parasite identified	P.falciparum	32	47.1%
	P.vivax	19	27.9%
	Mixed	6	8.8%
	Smear neg	11	16.2%

Table 5.4 Method of malarial diagnosis and type of parasite identified in patient visited WKUSTH in 2016

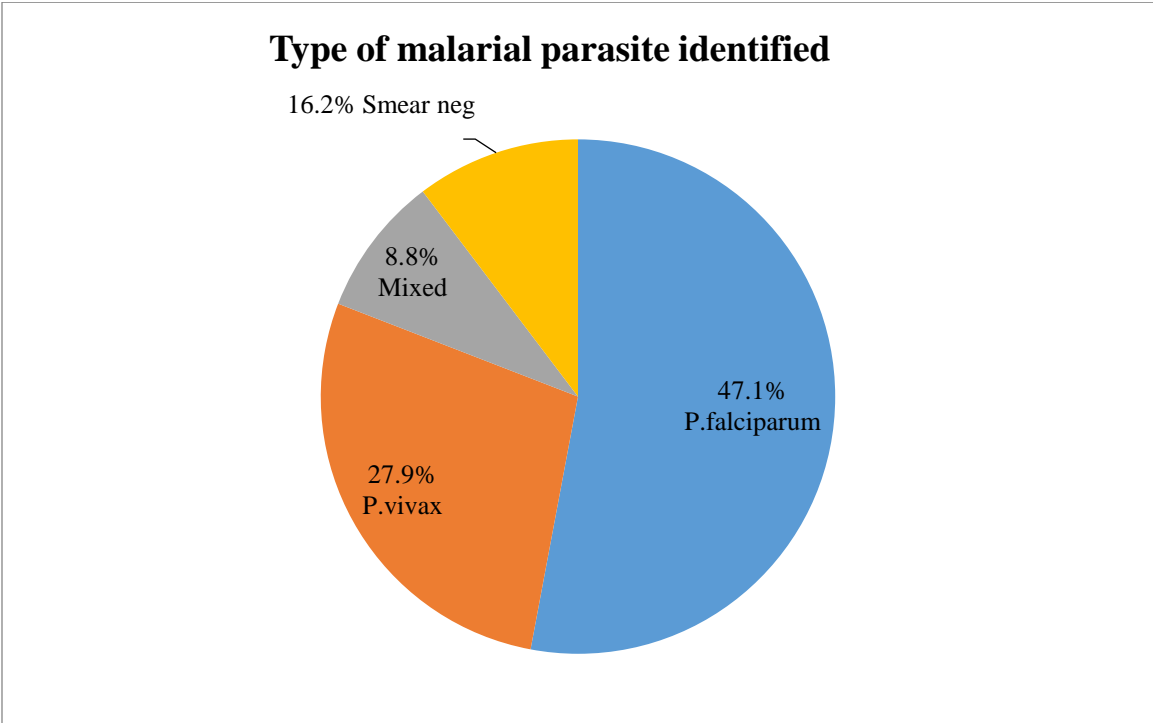


Figure 5.2 Type of parasite identified in malarial patient visited WKUSTH in 2016 E.C

5.5 Diagnosis of severe malaria and severity features

From our study those who was diagnosed with malaria(68) 29.4%(20) had severe malaria.

The common severity features of severe malaria seen were severe anemia 40%(8),Prostration 25%(5),cerebral malaria 15%(3) and Hypoglycemia 15%(3).

Variables		Frequency	Percentage
Diagnosis of severe malaria	Yes	20	29.4%
	No	48	70.6%
Severity features	Cerebral malaria	3	15%
	Sever anemia	8	40%
	Hypoglycemia	3	15%
	Prostration	5	25%
	other	1	5%

Table 5.5 Diagnosis of severe malaria and severity features

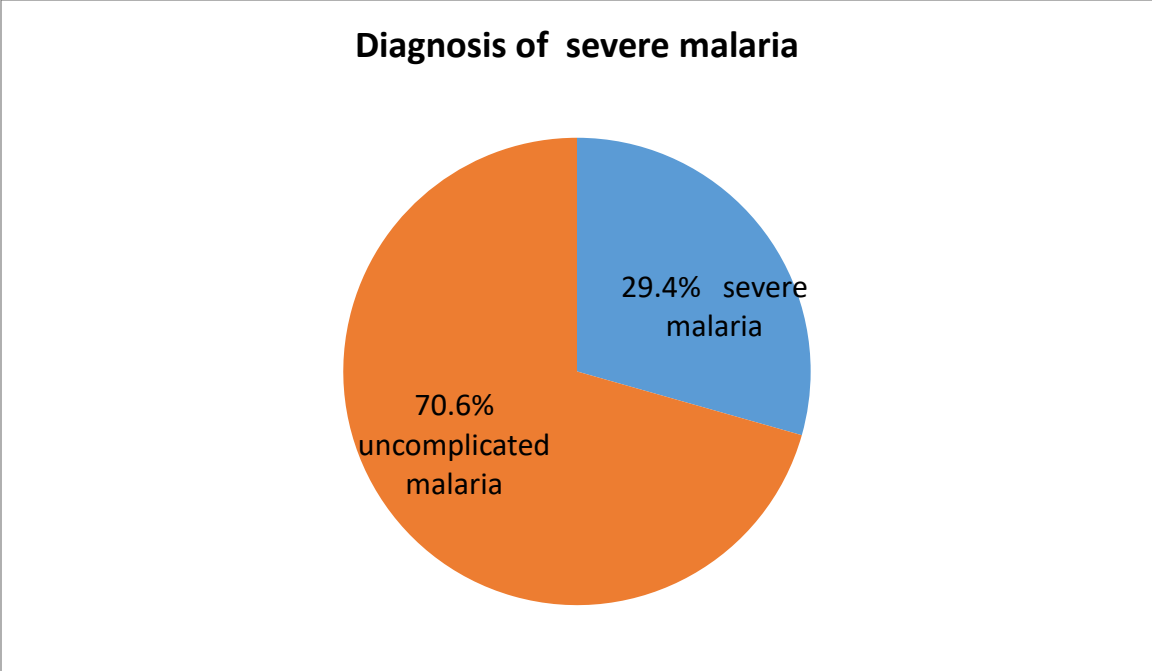


Fig 5.2 Diagnosis of severe malaria

5.6 Seasonality and previous malarial attack

Most of malarial cases occur in autumn 57.4%(39) especially in September and October and spring season 23.5%(16)

From those who had S.malaria about 70%(14) had previous history of malarial attack

From those who had S.malaria 15%(3) had comorbidity

Variable		Frequency		Percentage	
		Malaria	S.malaria	Malaria	S. Malaria
Season	Autumn	39	17	57.4%	85%
	Winter	3	-	4.4%	10%
	Summer	10	1	14.7%	5%

	Spring	16	2	23.5%	-	
Previous malarial attack	Yes	37	14	54.4%	70%	
	No	31	6	45.6%	30%	
Comorbidity	No	60	17	88.2%	85%	
	Yes	HTN	2	1	2.9%	5%
		DM	3	-	4.4%	-
		Other	3	2	4.4%	10%

Table 5.6 seasonality, history of previous malarial attack and comorbidity

5.7 Treatment of malarial patients

Most of malarial patient were provided with antipyretics 80%(53)

Three of patient with severe malaria received(15%) transfused with blood

All of patient with severe malaria treated with Artemisinin based combination therapy

Variables		Frequency	Percentage
Supportive treatment given	Antipyretics	53	77.9%
	Blood transfusion	3	4.4%
	Iv fluids	10	14.7%
	others	2	2.9%
Antimalaria that was given	Artemisinin based combination therapy	32	47.1%
	chloroquine	17	25%
	Quinine	19	27.9%

Table 5.7 Treatment of malarial patients at WKUSH in 2016

5.8 Duration of hospital stay and Treatment Outcome

35%(7) S.malaria patients had more than 3 days hospital stay. From patients diagnosed with severe malaria 20%(4) were died and 80%(16) fully recovered compared to other diagnosis that had 0.3% mortality rate

Variable		Frequency		Percentage	
		Malaria	S.malaria	Malaria	S.malaria
Duration of hospital stay	<3days	60	13	88.2%	65%
	>3days	8	7	11.8%	35%

Table 5.8 duration of hospital stay of malaria and S malaria patient

Variables		Frequency	Percentage
Treatment outcome of sever malaria	Recovered	16	80%
	Died	4	20%
Treatment Outcome of Malaria	Recovered	64	94.1%
	Died	4	5.9%
Treatment Outcome of Other disease	Recovered	328	97.9%
	Died	1	0.3%
	Other	6	1.8%

Table 5.9 Treatment Outcome of patient who was treated at WKUST in 2016

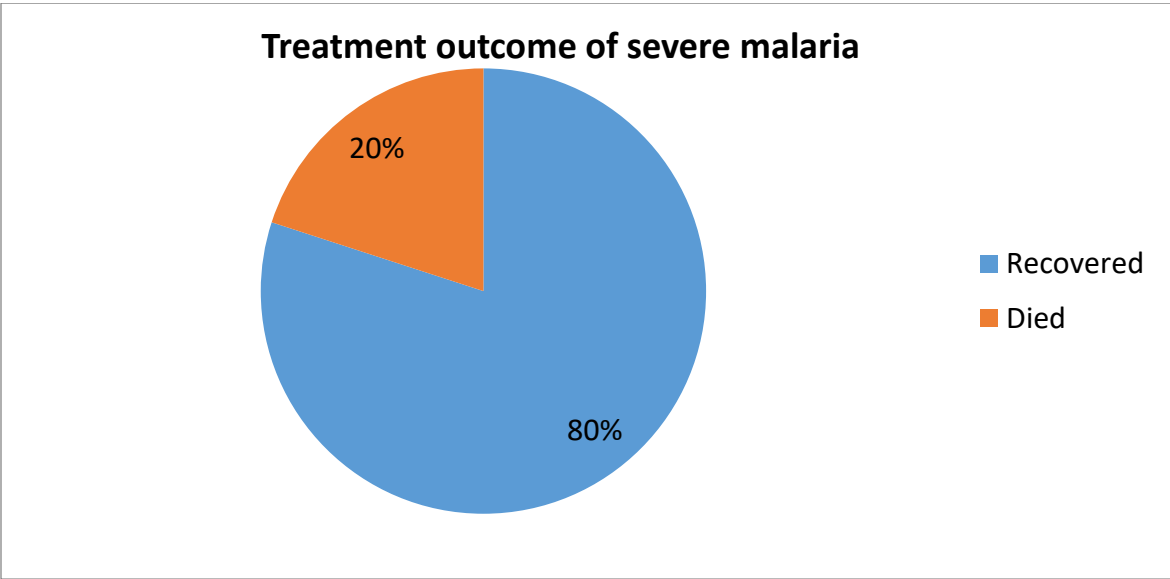


Figure 5.3 Treatment Outcome of severe malaria patients who was treated at WKUST in 2016 E.C

5.9 Factors Associated with severe malaria

All the variables which fulfilled the chi-square assumption were fitted into bi variable and multi variable logistic regression. Age, sex, seasonal variation, duration of symptom, duration of hospital stay, prior history of malaria, type of parasite, comorbidity, and other diagnosis fulfilled the variable screening criteria (p-value < 0.5) and entered into multi variable logistic regression analysis. Consequently, Age, sex, seasonal variation, duration of symptom, duration of hospital stay, prior history of malaria, type of parasite, co morbidity , were significantly associated with severe malaria at multi variable with less than 0.05 p values.

Accordingly, regarding sex it showed a significant association with the risk of infected with severe malaria. The odds of having severe malaria among male were 1.8 times higher as compared to females [AOR = 1.8; 95% CI (0.23-14)]. This study showed that those patients who came from rural area had 6 times higher odds of developing severe malaria as compared to those patient who came from urban area [AOR =6.05 CI[(0.68-53)]. Nevertheless, the odds of severe malaria among patients who presented after 72 hrs of

onset of symptoms had higher odds of developing severe malaria than those who presented in less than 72 hr of symptom onset. [AOR =1.24 CI [(0.077-20)].Those patients who presented during autumn season had relatively higher odd ratio of developing severe malaria than the remaining season [AOR =0.84 CI [(0.14-4.7)].

The odds of having severe malaria among those with prior history of malaria were higher than those patients without prior history. [AOR = 0.7; 95% CI [(0.12-4.3)]]. Regarding co-morbidity those who has co-morbidity had increased odds of developing severe malaria than those without co-morbidity [AOR = 1.8; 95% CI [(0.08-40)]]

Plasmodium falciparum was found to be the most dominant species in the study causing to almost all of the severe malaria cases [AOR = 1.38; 95% CI [(0.57-33)]].

Variables		Diagnosis of severe malaria N %		COR (95%CI)	P-value	AOR (95%CI)	p-value
		Yes	No				
Sex	Male	15(22.1%)	26(38.2%)	2.1(1.1-4.1)	0.014	5.5(1.8-16.5)	0.001
	female	5(7.4%)	22(32.4%)	1	1		1
Age	<15	2 (2.9%)	-	1	1		1
	15-30	9 (13.2%)	16(23.5%)	0.37 (0.07-1.8)	0.234	11(1.17-104)	0.038
	31-45	9(13.2%)	28(41.2%)				
	>46	-	4(5.9%)				
Residence	rural	19(27.9%)	14(20.6%)	1	1		1
	urban	1(1.5%)	34 (50%)	0.64(0.32-1.2)	0.207	3.2(1-9.9)	0.047
Type of parasite	P .f	19(31.1%)	17(27.9%)	2.2 (1.1-4.3)	0.012	6.3(2-19.9)	0.0
	p. v	1 (1.6%)	18 (29.5%)	1	1		1
	mixed	-	6(9.8%)				
	others	-	-				
Duration of presentation	24hr	1(1.5%)	7(10.3%)	1	1		1
	1-2day	14 (20.6%)	33 (48.5%)	11(2.6-51)	0.001	0.06(0.01-	0.001

						0.49)	
	.>=3day	5(7.4%)	8(11.8%				
comorbidity	Yes	3(4.4%	5(7.4%	0 (0-0)	0.001	0.47(0.02-10)	<0.001
	No	17 (25%	43(63.2%	1	1		1
Duration of hospital stay	<3days	13 (19.1%	47 69.1%	1		0.028(0.007-	0.0
	>=3 days	7 (10.3%	1 1.5%%	0.07(0.03-0.17)	0.0	0.115)	

Table 5.11: Bi variate and multivariate analysis of factors associated with magnitude of severe malaria in WUSTH IN 2016E.C

6.DISCUSSION

Malaria is one of the major public health agenda, specially, in endemic geographical settings. In Ethiopia clinical malaria incidence rate has dropped from an average of 43.1 case per 1000 population annually between 2001 and 2010 to 29 case per 1000 population between 2011 and 2016. Death associated with malaria has declined from 2.1 deaths per 100000 populations between 2001 and 2010 to 1.1 death per 100000 populations between 2011 and 2016. That was due to new policy of free malaria prevention and treatment which addresses the poor whom are more prone to the infection. (Malaria epidemiology and intervention in Ethiopia from 2001 to 2016).

The primary intention of this study was to assess the magnitude of severe and complicated malaria cases among patients admitted at WUSTH in 2016E.C.It is also necessary to identify associated factors influencing severe malaria and to reduce the risk of mortality and morbidity associated with the disease.

In present study ,among the 403 cases visiting WUSTH, the overall prevalence of malaria documented was 16.9%(n+68) from which severe malaria case was 20 (29.4%) ,the total prevalence was higher than reported from other retrospective studies conducted in Jimma university specialized hospital, the average annual severe malaria admission recorded was 2.6%(48/1863) and is slightly higher than annual general malaria caused hospital admission 16% reported from Oromia regional state (PMI,2015).The possible justification for this discrepancy might be due to the difference in the mode of report, our report involves all age groups where as

in Jimma, the report include only adult severe malaria admission while the report from Oromia regional state includes all age groups, the other possible explanation would be climatic and altitude differences.

In the current study the most common age category confirmed to be positive for malaria infection were adults between 15-45years () followed by children between 5 and 14 years old (23.5, n=16). [AOR = 1.8; 95% CI (0.23-14)]. The highest malaria prevalence in the adult age group obtained was in agreement with other findings reported across Ethiopia, like in Arba Minch primary hospital adult population age group between 18 and 40 (74.7%) are more presented with severe malaria similar to a study conducted in Gondar Referral hospital which is higher among age group 20 -45 (34.55%). This occurred most likely because of an active working age group which makes them vulnerable for an anopheles mosquito bite.

In the present study, sex had showed a significant association with the risk of infected with severe malaria. The odds of having severe malaria among male 22.1% (15) were 1.8 times higher as compared to females [AOR = 1.8; 95% CI (0.23-14)]. This finding was in contrast with the majority of study done in Ethiopia, where males were highly affected by malaria than females. According to the study conducted at Arba Minch primary hospital, males were 2.7 times more affected than females. [AOR = 2.7; 95% CI (0.825-9.33)]. The reason why malaria affected more males might be due to the fact that males engaged in activities outside their residence area, migration which make them more prone to infective mosquito bites as compared to female counter parts which are mostly at home and are not exposed counter parts which are mostly at home and are not exposed to malaria areas and protected from such infects bites.

The major annual transmission mode of severe malaria in this study has showed seasonal variation in which most cases occur in autumn which accounts 85% (N 17). Malaria transmission in Ethiopia is mainly seasonal and unstable character and area which with bimodal seasonal rain fall will have two major malaria transmission season. Thus, higher malaria transmission is recorded after heavy rain of summer September to December and then followed by March to May after the light rains, which agrees our findings. This was also in agreement with other studies done in the different part of Ethiopia. Variability of rainfall and temperature in each

season affects the availability of breeding habitats for mosquito vector, the length of mosquito larvae development and the rate of growth of the malaria parasites inside the vector.

The finding of this study revealed that the overall slide positivity was 83.8 % (57/68). It is higher than studies done in Gambella (49%) and Benshangul Gumuz (52%) regions stated in national figure of EMIS (46). The finding was also higher than studies conducted in Hadiya zone (47.2%)(49) and Jasikan district of Ghana(48). This difference may be attributed due to variation in climate, altitude, availability of perennial rivers that facilitate breeding of the parasite, and differences in malaria control interventions and intensity of malaria transmission among study setting and population.

P. f and *P. v* was found to be the most dominant species in the study area. According our study plasmodium falciparum caused 95% of severe malaria and plasmodium vivax caused 5% of severe malaria. The odd of developing severe malaria is 1.38 times higher in those infected with plasmodium falciparum than *p.vivax* [AOR = 1.38; 95% CI [(0.57-33)]]. This finding is similar to study conducted in Pawe hospital, Benishangul Gumuz Regional state; 76% predominance of *P. f* (68). Ethiopian national profile of malaria parasite distribution also provides similar result indicating *P. f* and *P. v* are the two dominant malaria parasites.

In this study the most common uncomplicated non-specific malarial symptoms presented were characterized by fever, chills, headache, aching and chills with other accompanied symptoms such as vomiting, rigor, shivering, cramp, nausea and anorexia with a large number of febrile cases. Compared to the study by Anstey et al. (2012) regardless of age and gender in the non-specific symptoms like headache, abdominal pain, fatigue and a non-fever phase (chills) occurs, followed by intermittent fever phase, The periodic fever phase is also known as “paroxysm” that occurs after the rupture of schizont-infected red cells (Anstey et al., 2012).

The most common documented severe malaria manifestations in this study were, severe anemia 40% (8/20), followed by prostration 25%(5/20) , cerebral malaria 20% (4/20),and hypoglycemia 10% (3/20).Some of these complications such as severe anemia, hypoglycemia, and cerebral malaria among children were reported from the same country (Ketema and Bacha, 2013). In this study hypoglycemia have been the most common severe complication observed in children less than 14// years old.

Regarding treatment outcome of SM 20% (4/20) was died the remaining 80% (16) were recovered and discharged. The current finding is higher than study conducted in Ibadan Nigeria 1.4% (33), Central India 4.9% (55), Kisangani town of democratic republic of Congo 3.4%(53), and Northern India 11.1%(54). However the current finding is lower than the finding of Uganda which is higher in children with cerebral malaria(33.3%) and severe anemia (25.5%)(35).This difference may be due to varying sample size, socio-economic, health seeking behavior and quality of comprehensive malaria control and management packages from country to country.

From clinical predictor's duration since onset of symptoms was found to be a significant predictor of treatment outcome of SM. In this study late initiation of treatment after 3 days of onset of symptoms was associated with 1.24 times higher odds of developing severe malaria than those who sought treatment earlier. [AOR =1.24 CI [(0.077-20)]. This finding is similar to multi-centered systemic review and meta-analysis study on the impact of progression of uncomplicated *P. f* malaria to sever malaria. Similarly study in Arba Minch General hospital, from September 2015- August 2018 revealed the same finding, where those who came after 4 days onset of symptoms had 2.2 times higher chance of developing severe malaria than those who sought treatment earlier.[AOR =2.23 CI [(0.64-7.74)]. This is due to the fact that when there is delayed initiation of treatment the stages of pathogenesis progress to advanced stage were routine therapy can not immediately produce effective Cure.

Regarding co-morbidity about 4.4% (3) of sever malaria had comorbidity illness, those who has co-morbidity has increased odds of developing severe malaria than those without co-morbidity. [AOR = 1.8; 95% CI [(0.08-40)]] The current finding is consistent with study conducted in Arba Minch generalized Hospital from September 2015- August 2018, were those with comorbidity had 13 times higher chance of developing severe malaria than those without comorbidity. [AOR = 13.16; 95% CI [(4.16-41.57)]] This is may be due to synergistic effect for mortality which affects multiple organ resulting in prolonged hospitalization and make diagnosis challenging.

7.Strength and weakness of the study

7.1 Strength of the study

This study will provide clinical insight to the magnitude severe malaria in clinical setting addressing the prevalence and treatment outcome of severe malaria in WUSTH.

This study included participants from all age group which are affected by malaria

7.2 Limitation of the study

The study was conducted in WUSTH. The scope of the study was limited to the Retrospective assessment of malaria in WUSTH. Due to time and budget it did not include the prevalence and incidence other than malaria.

The study is conducted in single hospital setting (WUSTH) Thus the findings may not be applicable to other regions of Ethiopia.

8. CONCLUSIONS AND RECOMMENDATIONS

8.1 Conclusion

Although prevalence of malaria seems decreasing due to intensive intervention and combined strategies approaches in the country, clinical data showed that, malaria is still a major health problem in the study area. Both *P. falciparum* and *P. vivax* were reported. Overall, *P. falciparum* was 47.1% followed by *P. vivax* 27.9% and mixed-infection cases 8.8%. Males were more affected than females. The highest malaria prevalence in age b/n 15 -45 yrs. The distribution of malaria showed seasonality with the highest prevalence in autumn followed by spring season. Severe malaria complications associated such as prostration, severe anemia, Cerebral malaria and hypoglycemia were observed in the study area. Regarding treatment outcome of Severe malaria 20% (4/20) was died the remaining 80% (16) are recovered and discharged.

8.2 Recommendation

- Seasonal variations require more focused attention to better control malaria transmissions and potential outbreaks.

- Community-based studies are recommended for better understanding of malaria transmission dynamic including delineation of risk factors.
- Furthermore, awareness creation activities that involve the community on prevention and control measure of the disease, on clinical symptoms of malaria and early seeking medication when they have malaria like symptom must be given.

REFERENCES

Abebe TN (2014). Compiled body of works in field epidemiology, MPH Thesis, School of Public health, Ethiopia field epidemiology training program, Addis Ababa University, Addis Ababa, Ethiopia

- Alemu A, Fuehrer HP, Getnet G, Tessema B, Noed H (2013). *P. ovale curtisi* and *P. ovale wallikeri* in North-West Ethiopia. *Malar J*; 12:346
- Baird JK (2013). Evidence and implications of mortality associated with acute *P. vivax* malaria. *Clin Microbiol Rev.*; 26:36–57.
- Bamaga OA, Mahdy MA1, Mahmud R, Lim YA (2014) Malaria in Hadhramout, a southeast province of Yemen: prevalence, risk factors, knowledge, attitude and practices (KAPs). *Parasite Vectors*; 7: 351.
- Clark HC (1915). The diagnostic value of the placental blood film in aestivo-autumnal malar. *J Exp Med*; 22: 427–45.
- Cot, Deloron (2003). Malaria prevention strategies: Pregnancy-Associated Malaria (PAM). *Br Med Bull* 67(1):137-48.
- Cox-Singh J (2008). *P. knowlesi* malaria in humans is widely distributed and potentially life threatening. *Clin. Infect. Dis.* 46: 165-171.
- FMoH (2000). Malaria control profile. Ministry of Health, Addis Ababa, Ethiopia, pp1-10
- FMoH, (2012), National Strategic Plan for Malaria Prevention, Control and Elimination in Ethiopia: 2011–2015, Addis Ababa, Ethiopia
- Gebremariam N (1988). The ecology of health and disease in Ethiopia in Malaria. Edited by Kloos H, Zein AZ. *Boul Westview Press*; 136-150.
- Getachew, F., Abiyu W, Alemtegn G, Ali A, Tarekegn H, Yenus A, Belay T, Yitayih W, and Abebe A (2013). Prevalence of malaria from Blood Smears Examination: A seven-year Retrospective study from Metema Hospital, North West Ethiopia. *Malaria Research and Treatment*; 2013, article ID 704730
- Gething PW, Patil AP, Smith DL (2011). A new world malaria map: *P. falciparum* endemicity in *Malar Edited*; 556-576.
- Ghebreyesus TA, Derressa Witten KH, Getachew A, Seboxa T (2006). The epidemiology and ecology of health and disease in Ethiopia, *In Malar Edited*, 556-576
- Greenwood BM., Bojang K., Whitty CJ and Targett GT (2005). JCI Malaria progress, perils and prospects for eradication, *Malar Lancet*; 365 (9469), 1487–98.
- Griffin JT, Hollingsworth TD, Okell LC, Churcher TS, White M, Hinsley W, Bousema T, Drakeley CJ, Ferguson NM, Basáñez MG, Ghani AC (2010). Reducing *P. falciparum* malaria transmission in Africa: a model-based evaluation of intervention strategies; *Med*, 7:e1000324.
- Kassa M, Sileshi M, Mohammed H, Taye G, Asfaw M. (2005) Development of resistance by *Plasmodium falciparum* to sulfadoxine/pyrimethamine in Amhara region, Northwestern Ethiopia, *Ethiop Med J*.;43:181–7.
- Khattak AA, Venkatesan M, Nadeem MF, Satti HS, Yaqoob A, (2013). Prevalence and distribution of human Plasmodium infection in Pakistan. *Malar J*, 12: 297
- Lindsay SW, Martens WJM (1998). Malaria in the African highlands: Past, present and future. *Bull World Health Organ*; 76(1):33–45.

- May RM and Anderson RM (1990). Parasite-host co-evolution. Review [50 refs]. *Para 100 Supp*: S89-101.
- Mekonnen, SK, Aseffa A, Berhe N, Teklehaymanot T, Clouse RM., Gebru T, Medhin G, Velavan TP(2014). Return of chloroquine-sensitive *Plasmodium falciparum* parasites and emergence of chloroquine-resistant *Plasmodium vivax* in Ethiopia. *Malar. J.* 13: 244.
- Mengistu, H. and Solomon, G. (2014).Trend Analysis of Malaria Prevalence in Arsi Negelle Health Center, Southern Ethiopia, *Acad. J.* vol.7(1), 1-6
- MI. Africa IRS (AIRS) (2016) Project Indoor Residual Spraying (IRS 2) Task Order Six. Ethiopia 2016 End of spray report. Bethesda, MD: *Abt Associates Inc.*
- Ministry of Health (2010). National strategic plan for malaria prevention, control and elimination in Ethiopia,2011–2015. Addi Ababa: Ministry of Health of Ethiopia;
http://www.nationalplanningcycles.org/sites/default/files/country_docs/Ethiopia/ethiopia_malaria_national_strategic_plan_2011-2015_130810.pdf. Accessed 21 July 2021.
- Mockenhaupt FB, Ulmen U, von Gaertner C, Bedu-Addo G, Bienzle U (2002). Diagnosis of placental malaria. *J C lin Microbiol; 40:306–malariology*. 4th ed. London: Arnold; 2002. p. 85–106.
- Nega D., Assefa A., Mohamed H., Solomon H., Woyessa A., Assefa Y., Kebede A., Kassa M. (2016). Therapeutic efficacy of artemether-lumefantrine (Coartem) in treating uncomplicated *P. falciparum* Malaria in Methahara, Estern Ethiopia. *Reg cli sty. PLoSOne 11(4): e0154618*
- WHO. (2010). Guidelines for the Treatment of Malaria, 2nd edn.. World Health Organization, Geneva.
- WHO. (2022). *World Malaria Report*. Geneva, Switzerland.
- WHO. (2022) World malaria report. World Health Organization, Geneva.
- WHO. (2014). Tropical Medicine and International Health is published by John Wiley & Sons., 19 (Suppl. 1), 7–131.

Annex

Data collection format for Retrospective Analysis of Malaria

Section A: Patient Demographics

1. Medical Record Number: _____

2. Age (in years): _____

3. Gender:

- Male
- Female

4. Residence

- Urban
- Rural

Section B: Clinical History

5. Date of Admission: _____

6. Date of Discharge: _____

7. Presenting Symptoms: (Check all that apply)

1. Fever
2. Chills
3. Headache
4. Nausea/Vomiting
5. Sweating
6. Fatigue
7. Joint/Muscle pain
8. Other: _____

Duration of Symptoms Prior to Admission (days): _____

Section C: Diagnosis and Lab Results

9. Malaria diagnosis

1. Yes
2. No

IF NO skip to question no.10. If yes

9.1 Malaria Diagnostic Methods

1. Microscopy
2. Rapid Diagnostic Test (RDT)
3. smear negative

9.2 Type of Malaria Parasite Identified (if applicable):

1. Plasmodium falciparum
2. Plasmodium vivax
3. Mixed infection
4. other

9.3 diagnosis of severe malaria

1. Yes
2. NO

If yes

9.3.1 severity features _____

9.4 Treatment and Outcome

1. Recovered
2. Died

9.4.1 Antimalarial Treatment Administered:

- Artemisinin-based combination therapy (ACT)
- Chloroquine
- Quinine
- Other: _____

9.4.2 Supportive Treatment Provided (if any):

- Antipyretics
- Blood transfusion
- IV fluids
- Other: _____

9.5 Treatment Outcome:

- Recovered
- Referred to another facility

- Death

- Other: _____

9.6 Comorbid Conditions Identified: (Check all that apply)

HIV/AIDS

Malnutrition

Tuberculosis

Hypertension

Diabetes

Other: _____

9.7 History of Previous Malaria Episodes:

- Yes

- No

9.8 Season of Admission:

Autumn

Summer

Spring

Winter

10. If answer to Q no 9 is no

10.1 What is the other diagnosis _____

10.2 Treatment Outcome:

- Recovered

- Referred to another facility

- Death

- Other: _____