ANTIMALARIAL USE IN MAJOR PUBLIC HOSPITALS IN ELDORET TOWN: REVIEW OF USE IN UASIN GISHU AND HURUMA COUNTY HOSPITALS AND MTRH

DR. MATALA WAFULA

W64/69535/2013

A dissertation submitted in partial fulfillment of the requirements for the award of the degree of Masters of Science in Tropical and Infectious Diseases at the University of Nairobi

Declaration

I declare that this is my original work and to the best of my knowledge has not been presented anywhere else for consideration.

Investigator: Dr. Matala Wafula é é é é é é .....

Supervisor: Professor Anastasia N. Guantai.....

Professor of Pharmacology and Therapeutics

School of Pharmacy, University of Nairobi

DEDICATION

To Audrey, my daughter.

ACKNOWLEDGEMENT

First, I thank Almighty God for giving me strength and perseverence and seeing me through this project.

I wish to acknowledge the assistance, guidance and direction accorded to me by my supervisor and role model, Professor A. N. Guantai.

Finally, to all my friends for their time, wise counsel and support. God bless you all.

ABSTRACT

Background; Rational use of antimalarials advocates for correct dosages calculation, intervals and completion. The World Health Organization Guidelines for the treatment of malaria provides evidence-based and up-to-date recommendations for countries on malaria diagnosis and treatment which help in the formulation of policies and strategies. The Guidelines cover the diagnosis and treatment of uncomplicated and severe malaria caused by all types of malaria parasites.This includes treatment of malaria in special groups (young children, pregnant women, HIV /AIDS), in travellers (from non-malaria endemic regions) and in epidemics and complex emergency situations. However there is paucity of information on rational use of antimalarials in Kenya.

Methods; A cross sectional descriptive study was conducted at Uasin Gishu and Huruma county hospitals and Moi Teaching and Referral Hospital (MTRH). All antimalarial prescriptions and treatment sheets in the month of April were evaluated.

Results: Laboratory and clinical method of diagnosis accounted for 63% and 37% respectively of all the cases. Blood smear method represented 71% while Rapid Diagnostic Test (RDT) represented 29%. Main antimalarials prescribed were Artemether/Lumefantrine (60.2%) and Artesunate injection (29.3%). Antimalarial agents use among the special groups was in line with the current national guidelines.

Conclusion: The national guidelines on malaria treatment and management are not being fully followed in the major Uasin Gishu county hospitals and MTRH.

ABBREVIATIONS.

ACTs:	Artemisinin-based combination therapies
ASAQ:	Amodiaquine + Artesunate
DHAPQ:	Dihydroartemisinin + Piperaquin
DOA	Duration of Action
ELISA:	Enzyme-linked immunosorbent assay
IFA:	Indirect immunofluorescence
MTRH:	Moi Teaching and Referral Hospital
RDTs	Rapid diagnostic tests
SJS:	Steven Johnson Syndrome
SP:	Sulfadoxine/Pyrimethamine
WHO	World Health Organization

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CHAPTER 1: INTRODUCTION.

1.1 (a) Background

Malaria is a leading cause of morbidity and mortality in Kenya and accounts for 30-50% of all outpatient attendance and 20% of all admissions to health facilities. Approximately 170 million working days are lost to the disease each year. Malaria accounts for almost 20% of all deaths in children under five. Pregnant women and children under 5 years of age are considered the most vulnerable group to malaria infections (Kenya Malaria Fact Sheet, 2014).

In Kenya, the main causative agent of malaria is *Plasmodium falciparum*. Uasin Gishu county is zoned as a malaria epidemic prone area, as it is part of western highlands of Kenya. Therefore, malaria transmission in this region is seasonal but with considerable year to year variation. Unlike malaria endemic regions, the whole population in this region is vulnerable and case fatality rates during an epidemic can be up to ten times greater than those experienced in regions where malaria occurs regularly (National Guidelines for the Diagnosis, Treatment and Prevention of Malaria, 2012). The national guidelines ephasize that peripheral parasitaemia should be the gold standard in diagnosis of malaria since the government provides rapid diagnostic laboratory test kits, train personel and provide free antimalarials.

The Kenyan Ministry of Health developed guidelines for malaria diagnosis, treatment and prevention with an aim of improving malaria case management by all health workers and having a harmonized approach in efforts aimed at the reduction of morbidity and mortality

due to malaria. The 4th edition emphasizes on diagnosis based treatment of malaria and artemisinin based combination as first line treatment for uncomplicated malaria in Kenya.

Classes of anti-malarials are:

i. **4-Quinoline methanols** e.g. Quinine, Quinidine and Mefloquine. Have blood schizontocidal and weak gametocytocidal effects. Accumulated in the food vacuoles of Plasmodium species and inhibit the hemozoin biocrystallization thus facilitating an aggregation of cytotoxic heme.

ii. **4-aminoquinolines**: e.g. Chloroquine, Hydroxychloroquine and Amodiaquine. They induce oxidant stress, prevent nucleic acid synthesis and consequently protein synthesis in the rapidly dividing erythrocytic forms of malaria parasites.

iii. **Antifolates:** e.g. proguanyl, sulphonamides, trimethoprim and pyrimethamine. Inhibit synthesis of folic acid in plasmodium. Sequential blockage of folic acid synthesis at two different stages achieved by combination of a sulphonamide and pyrimethamine. Most notable side effect of sulphonamides is the Steven Johnson Syndrome (SJS).

iv. **Artemisinin and derivatives:** Concentrate in the infected red blood cells. They interfere with the integrity of the parasite membranes causing lysis and induces significant oxidant stress making the environment unfavourable for growth and multiplication of the erythrocytic forms of the malarial parasite. They interfere with DNA replication, nucleic acid and protein synthesis, conversion of heme to hemozoits and induces parasite clumping. The drug also concentrates in the food vacuoles of the parasites and interfere with mitochondrial function. Derivatives of artemesinin aim at increasing the potency, pharmacological parameters and decreasing the resistance to the compound. Ether derivatives are more potent than artemesinin but weaker than dihydroartemesinin derivatives. Ester derivatives are more potent than the dihydroartemesinins. Carbonates

are the most potent. Artemesinin has a short duration of action, hence combined with Lumefantrine, an antimalarial with long duration of action.

v. **8-aminoquinolines**: e.g. Pamaquine, pentaquine, isopentaquine, primaquine and quinocide.

vi. **Atovaquone:** Plasmodium parasites are unable to utilize pyrimidines from the salvage pathway hence must synthesise them de novo. One of the enzymes involved here, Dihydro-Orotate Dehydrogenase, is inhibited by Atovaquone.

vii. **Amino alcohols:** e.g. Halofantrine. Has a long duration of action. It Undergoes slow erratic dose related absorption after oral administration. Absorption is increased by fatty diet.

viii. **Antibiotics** e.g. Doxycycline and Clindamycin.

1.1(b) Resistance to anti-malarial agents.

Anti-malarial drug resistance is the ability of a parasite to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within tolerance of the subject. The drug in question must gain access to the parasite or the infected red blood cell for the duration of the time necessary for its normal action, excluding all cases where anti-malarial prophylaxis has failed.

Drug resistance may lead to treatment failure, but treatment failure is not necessarily caused by drug resistance despite assisting with its development.

The generation of resistance varies between plasmodium species and is initiated through spontaneous mutation.

Factors promoting the spread of resistance to antimalarial drugs.

1. Biological factors e.g. in the immunocompromised individuals, pregnant women and young children.
2. The treatment regime prescribed i.e. drug intake, combination, interactions and the drug's pharmokinetic and dynamic properties.
3. Pharmokinetics: Drugs with shorter half-life's require more frequent administration to maintain the correct plasma concentrations presenting more problems if levels of adherence and compliance are unreliable.
4. The use of anti-malarials developed from similar basic chemical compounds e.g. cross-resistance to chloroquine and amiodiaquine.
5. The pharmokinetics of the individual anti-malarial drugs in a combined formulation.

1.1(c) Artemisinin-based Combination Therapy (ACTs)

Combination therapy is the simultaneous use of two or more drugs with independent modes of action. ACTs prevent resistance development, have very rapid reduction in the parasite biomass with an associated reduction in clinical symptoms and reduction in the transmission of gametocytes thus decreasing the potential for the spread of resistant alleles. ACTs include

1. Artesunate plus Amodiaquine or Mefloquine or Sulphadoxine/Pyrimethamine or Pyronaridine.
2. Artemether plus Lumefantrine.
3. Dihydroartemisinin plus Piperaquine.

All these combinations are recommended by the WHO for management of uncomplicated falciparum malaria (WHO, 2010)

1.1 (d) Parasitological diagnosis of malaria.

All patients with fever or history of fever should be tested for malaria and only patients who test positive should be treated. Futhermore, all patients should be assessed for other conditions that may cause fever and be managed accordingly.

Current laboratory diagnosis of malaria is either by microscopy or RDTs. In microscopy, thin and thick blood smears are obseved for *Plasmodium* species identification and parasite quantification respectively. RDTs are immunochromatographic tests based on detection of specific parasite antigens. Can test for histidine rich protein 2 (HRP2) specifically for Plasmodium falciparum or parasite lactate dehydrogenase (pLDH) or aldolase for all the plasmodium species that cause malaria. Other methods to detect parasites include Polymerase Chain Reaction (PCR) that detects the *Plasmodium* parasites DNA and serological tests that detects antibodies against malaria parasites using either indirect immunofluorescence (IFA) or enzyme-linked immunosorbent assay (ELISA). However, serology does not detect current infection but rather measures past exposure.

1.2. PROBLEM STATEMENT

Rational use of antimalarials is extremely important as injudicious use can adversely affect the patient, cause emergence of antimalarial resistance and increase the cost of health care. In Kenya, there lacks data showing a relationship between antimalarial drugs consumption and actual peripheral *Plasmodium* parasitaemia. Eldoret Town being a malaria epidemic region, malaria cases should be reported occassionally but the number of patients prescribed antimalarials throughout the year is high. Therefore, there could be wastage of antimalaria

drugs if those not requiring them are given due to wrong diagnosis besides being exposed to unwanted side effects of these drugs.

RESEARCH QUESTION

This study helps answer the following questions:

Do all patients being prescribed antimalarials need them, and if so are the antimalarials being prescribed correctly?

1.3 JUSTIFICATION

Eldoret Town is a malaria epidemic prone area of western highlands of Kenya.

Malaria disease has clinical symptoms similar to many other diseases thus syndromic management alone can lead to a malaria-free patient being treated for malaria. This contributes to irrational use of antimalarial drugs and hence encourage development of resistance, exposure of patients to unnecessary side effects of antimalarials and wastage of resources.

This study aimed at establishing methods by which malaria diagnosis is arrived at and how antimalarials are prescribed in major public hospitals of Eldoret Town. With the National Guidelines insisting on presence of peripheral parasitaemia as proof of malaria, this study sought to establish if this is the case in county hospitals of Eldoret Town. Futhermore, the National guidelines has in place first line and second line antimalarial drugs. This study establishes if indeed these are the drugs being given and if in their right dosages too.

1.4 STUDY OBJECTIVES

Broad Objective.

To determine the usage of antimalarials in major public hospitals in Eldoret Town .

Specific Objectives:

In major public hospitals in Eldoret Town, the study sought:

1: To document the procedures applied in reaching confirmatory diagnosis of malaria.

2: To determine the commonly used antimalarial agents and prescribing instructions.

3: To establish if malaria management is informed by national guidelines.

CHAPTER TWO: LITERATURE REVIEW

Complex societal issues like the misuse of antimalarials by healthworkers and the public and inconsistence supply of good quality drugs or insufficient surveillance play a largely unmeasured role that requires study and solutions.

Antimalarial drugs research at the Bangkok Hospital for Tropical Diseases recommends drug combinations for all adult patients suffering from acute uncomplicated falciparum malaria contracted in multidrug resistant areas. In severe malaria and malaria in children, the research concludes that drug combinations need further investigation (Looareesuwan *et al.* 1998).

Emergence of artemesinin-resistant malaria in western Cambodia is worrying. Genetically determined artemisinin resistance in *P. Falciparum* emerged along the Thailand-Myanmar border around 2004 and it has inceased substantially and will reach the rates reported in Cambodia soon. Concerted international efforts and stratergies to contain this hugely depends on whether or not the resistance has occured elsewhere (Aung *et al,* 2012). Therefore, despite their huge potential to reduce transmission, ACTs cannot be relied on to prevent it altogether. New approaches have been proposed, including coadministration of ACTs with primaquine (a drug with broader gametocytocidal properties than the artemisinins), and these have been shown to produce a substantial reduction in gametocyte carriage, compared with ACTs alone (Price, 2013).

The high use of antimalarials by health facilities and pharmacies participating in a study on irrational use of antimalarials in rural areas of eastern Parkistan contrasted sharply with the lack of malaria and vector in this area during the study period. Therefore there is need of training of health care personel and use of laboratory diagnosis worldwide in malaria to ensure resources are not misused or unnecessarily expose individuals to toxic effects of drugs (Khan *et al.* 2012).

Some antibiotics can also be used as antimalarial agents. Azithromycin in combination with artemisinin derivatives or quinine exerts additive to synergistic antimalarial interactions,

shows no cross-sensitivity with traditional antimalarials and has substantial antimalarial activity on its own (Harald *et al*. 2006). Clindamycin has antimalarial activity too but is not an ideal antimalarial regimen because of the need for twice-daily dosing and it is expensive. However, for the target population (children and pregnant women), quinine plus clindamycin is an extremely useful antimalarial combination (Bertrand and Peter, 2002).

Afghanistan has a much lower incidence of malaria than Africa, yet fever was substantially misdiagnosed as malaria in most cases. This was mainly due to false positive laboratory diagnoses of malaria and the clinicians disregard of negative slides results. Potentially fatal cases of malaria that occur rarely were not detected, emphasizing the role of RDTs. (Leslie *et al*. 2012)

Artemisinin with piperaquine given as a 2-day course is associated with late recrudescence within the 28 days of hospital observation. In contrast 3-day regimens with artemisinin-piperaquine and dihydroartemisinin-piperaquine has cure rates of over 98% and are well tolerated. Therefore both combinations represent potential alternatives to artesunate-mefloquine and artemether-lumefantrine and deserve further evaluation, including better pharmacokinetic characterizations of these combinations, additional studies in children and pregnant women, and carefully conducted field trials (Srivicha *et al.* 2007).

Combination of Atovaquone and Artemisinin shows additive activity to synergism against P. Falciparum strains while the combination of Quinine and Artemisinin shows clear synergism. Since quinine and mefloquine both belong to the quinoline methanol class and both show synergistic activity with artemisinin, it may be concluded that artemisinins are synergistic with the quinoline methanol group of compounds (Gupta *et al.* 2002)

Artemisinins are effective and unlikely to be cause of foetal loss or abnormalities when used in late pregnancy. However, none of the previous studies had adequate powers to rule out rare serious adverse effects even in the 2nd and 3rd trimesters and there is not enough evidence to effectively assess the risk-benefit profile of artemisinin compounds for pregnant women especially for the 1st trimester exposure. Therefore methodologically rigorous larger studies and post-marketing pharmacovigilance are urgently required (Dellicour *et al.* 2007).

A head to head comparison of four Artemisinin-Based Combinations for treating uncomplicated malaria in seven sub-saharan africa countries children found that AL, ASAQ and DHAPQ had excellent efficacy, up to day 63 post treatment. The risk of recurrent

infections was significantly lower for DHAPQ, followed by ASAQ then AL. This supports the recommendation of DHAPQ as a valid option for the treatment of uncomplicated *P. falciparum* malaria (DôAllesandro *et al*, 2011). Similar research showed that ASAQ and AL are both highly efficacious treatments for uncomplicated falciparum malaria in Nimba County, Liberia. Since 2010, ASAQ FDC was adopted as national first-line treatment in Liberia (Schramm *et al*, 2013).

Treatment regimens of Amodiaquine combined with sulfadoxine/pyrimethamine versus artemisinin-based combinations for the treatment of uncomplicated falciparum malaria are safe and well tolerated. The analysis further recommends that Amodiaquine+ Sulphadoxine/Pyrimethamine should be considered in some settings before the full implementation of an ACT (Obonyo *et al.* 2007). However, in Nigeria it was found that the combination of artesunate plus amodiaquine is therapeutically superior to a combination of chloroquine plus pyrimethamine-sulfadoxine, and significantly reduced gametocyte carriage following treatment (Sowunmi *et al.* 2005).

Artesunate-mefloquine regimen is well tolerated and is as effective as AL for the treatment of *P. falciparum malaria*. It also prevents more new infections (Sagara *et al*, 2008). Futhermore, the paediatric Artesunate + Mefloquine formulated in granule fixed dose combination is well adapted to children in Africa (Faye *et al,* 2010). This is further supported by findings in Cote dôIvore which concluded that Artesunate-Mefloquine paediatric formulation is safe and as effective as AL for treatment of uncomplicated malaria (Berenger *et al,* 2011).

The decline in malaria episodes in Africa calls for a shift from presumptive treatment to laboratory confirmed diagnosis and treatment in all areas, regardless of age and level of malaria transmission. This is feasable due to RDTs. Renewed malaria control involves improved clinical management and abandonment of irrational use of drugs (DôAcremont *et al.* 2009).

In Ugandan children it was found out that the effectiveness of a seven day course of quinine for the treatment of uncomplicated malaria was significantly lower than that of artemether-lumefantrine. Therefore, another artemisinin based combination therapy would be more appropriate to treat uncomplicated malaria even after initial treatment failure with an artemisinin based combination therapy (Achan *et al.* 2009). However, she concludes in a different article that in the near future, quinine will continue to play a significant role in the management of malaria, particularly in resource limited settings especially during the first trimester in pregnacy (Achan *et al.* 2011). On the other hand, a different study in Uganda

recommends that since DHAPQ is highly efficacious and less dosing compared to AL, it should be considered for a role in the antimalarial treatment policy of Uganda (Yeka *et al*, 2009).

In comparison to quinine, artesunate substantially reduces mortality in african children with severe malaria. Futhermore, parenteral artesunate should replace quinine as the treatment of choice for severe falciparum malaria worldwide (Arjen *et al*. 2010). Artemisinin derivatives are also not inferior to quinine in preventing death in children with cerebral malaria (Hmwe and Eduardo, 2009).

Malaria is commonly overdiagnosed in Tanzania in those presenting with febrile illness, especially in those in areas with low to moderate transmission and in adults. This has lead to cases of failure in treating the alternative cause of febrile illness. Therefore, diagnosis need to be improved. Also, routine hospital data may overestimate mortality from malaria as data used will include those who actually donôt have malaria (Reyburn *et al.* 2004).

In Tanzania it was found that failure rates with monotherapy were very high but the two combinations (Amodiaquine + Atesunate and Amodiaquine + Sulphadoxine+ Pyrimethamine) tested were efficacious and appeared safe. The findings also showed that efficacy in pregnancy is different from that in children (Mutabingwa *et al*. 2009). Malaria significantly increases the risk of miscarriage which can be prevented using the right antimalarial drug (McGready *et al*. 2012).

Despite the Tanzania government efforts to increase public awareness in the use of AL as first line treatment of uncomplicated malaria, irrational prescribing and dispensing is still rampant. Regular on-the-job training and continuing education should therefore be provided to drug dispensers and prescribers in public health facilities (Kamuhabwa and Silumbe, 2013).

Kenya, like many other African countries, is still far from achieving the Abuja targets. Government, with support from donors, should invest adequately in mechanisms that promote access to effective malaria treatment. Such approaches should focus on factors influencing multiple dimensions of access and will require the cooperation of all stakeholders working in malaria control (Chuma *et al.* 2009).

A combination of AL or DHAPQ are efficaceous in treatment of uncomplicated *P. Falciparum* as it was found among children in Western Kenya. Clearance rates of nearly

100% by day three of treatment is observed and lack of evidence of delayed parasite clearance indicates no emerging artemisinin resistace (Agarwal *et al*, 2013). Another study in Mbita in Kenya found out that DHAPQ regimen has a longer prophylactic time after treatment whereas gametocyte carriage and malaria transmission to mosquitoes is lower after AL treatment (Bousema *et al*, 2013).

All health facilities in Rachuonyo District in Kenya, were using general-purpose trucks to transport antimalarial drugs and did not have functional wall thermometers and that 87% of health care providers did not check storage conditions of drugs upon reception. Futhermore, 97% of the health care providers used physical examination for clinical diagnoses. It was also found that 13% of health care providers had no idea that antimalarials suspensions can undergo fermentation when not properly stored. Only 40% of the selected health facilities had current recommended antimalarial treatment drugs in stock. Therefore, management, administrative factors and policy issues could be a leading cause of antimalarial drug resistance and a case control study to explore the exact extent of drug resistance in this population in relation to the identified factors is urgently recommended (Angira *et al,* 2010).

Symptomatic diagnosis of malaria overestimates prevalence of malaria, but underestimates the prevalence of anaemia in children due to malaria, yet malaria induced anaemis still occurs frequently. Therefore, laboratory should confirm the presence of parasites for all suspected cases of malaria which can be achieved through RDTs and/or microscopic analysis (Choge *et al*. 2014).

CHAPTER THREE: METHODOLOGY

3.1 Study location

Uasin Gishu and Huruma county hospitals and Moi Teaching and Referral Hospital (MTRH) were the study locations. Uasin Gishu County is in western Kenya with Eldoret Town as its main administrative and commercial centre. By road, Eldoret Town is 310 kilometers from Nairobi, Kenyaôs capital city. MTRH is the second National Referral Hospital in Kenya after Kenyatta National Hospital, serving as the main referral centre of cases from the former Western, Rift Valley and Nyanza provinces. The Hospital is located along Nandi Road in Eldoret town. It borders Moi University School of Medicine, and is also its teaching hospital.

Uasin Gishu county hospital is located along Eldoret Malaba road, at the heart of Eldoret Town opposite Zion Mall.

Huruma sub-county hospital is located along Eldoret-Kitale Highway opposite Mwanzo Estate.

Uasin Gishu County has a population of 894,179 according to 2009 census and is pyramid shaped i.e. the numbers decrease with increase in age.

Malaria test positivity rate in 2011 was 30.2% and 25.8% in 2012. Malaria cases per 100,000 people was 24,271 in 2011 and 23,028 in 2012 according to health policy project website. From the same data, Kisumu, a malaria endemic region, had a malaria test positivity rates of 40.8% and 36.6% for 2011 and 2012 rrespectively, and malaria cases per 100,000 people of 49,384 ans 41,752 for 2011 and 2012 respectively. This shows cases of malaria and subsequent use of antimalarial drugs in Uasin Gishu County should be very low, which is not the case.

The county enjoys two rainy seasons with annual rainfall ranging between 900mm to 1200mm, with the wettest months being April and May. The driest months are January and February. The county is on a plateau and has a cool and temperate climate with annual

temperatures ranging between 8.4 degrees and 27 degrees Ceelcius (Kenya Information Guide). This climate justifies Uasin Gishu County to be a malaria epidemic region with malaria episodes being highest during rainy seasons.

3.2 Study design

The design used was cross sectional descriptive study.

3.3 Variables

Dependent variables

Laboratory diagnosis methods.

Independent variables

Antimalarial agents available.

3.4. Sample population

All outpatients and inpatients with prescription for antimalarials obtained from the county hospitals of Huruma and Uasin Gishu and MTRH were involved in the study during the month of April.

Inclusion Criteria.

All patients prescribed antimalarial drugs at the study sites within the month of April.

Exclusion Criteria.

Individuals self medicating antimalaria drugs i.e. those who acquied antimalarial drugs without prescription.

Prescriptions and laboratory results from private hospitals.

3.5 Sampling technique

Data on in-patients on antimalarials was obtained from the patientôs files. Information on whether or not there was a laboratory diagnosis of malaria was proved by the laboratory request form in the file. Information on antimalarial agent, dosage and route of administration of the same was obtained from the treatment sheet in the file.

Information on diagnosis, antimalarial agent and dosage to the outpatient was obtained from the prescription being presented and compared to the laboratory register to ascertain whether or not malaria test was performed.

Information obtained was captured on the questionnaire (Appendix 1) by the research assistant.

3.6 Sampling size.

All antimalarial prescriptions and treatment sheets seen at MTRH and county hospitals for a period of four (4) weeks and meet the inclusion criteria constituted the sample.

3.7 Data Management and quality checks

Quality control

Training and supervision of data collectors was carried out routinely. There was daily random checks, review for missing data, cleaning of data and counter checks on data entry.

CHAPTER FOUR: RESULTS AND FINDINGS

Table 1: Number of participants from each hospital.

Hospital	Frequency	Percent
MTRH	92	23.7
Uasin Gishu	202	51.9
Huruma	95	24.4
Total	**389**	**100**

Slightly more than half the patients prescribed anti malarial drugs at the study sites within the study period were from Uasin Gishu hospital 52% while those from Huruma and MTRH represented 24% each.

Figure 1: Proportion of participants from each hospital.

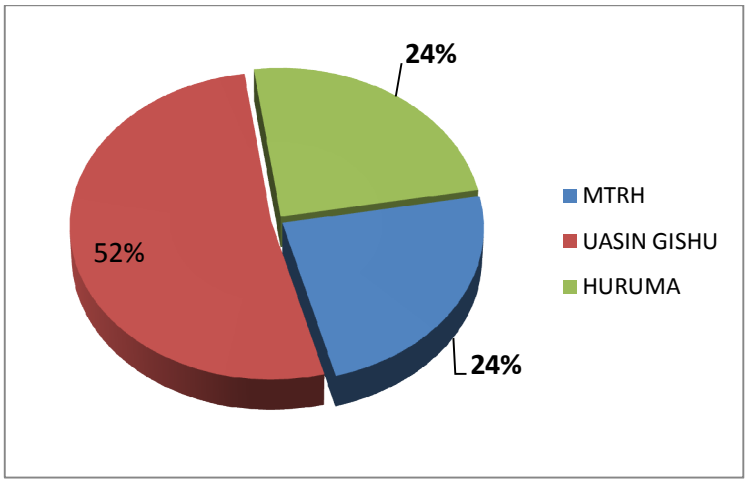

Table 2: Overal gender participation in the study.

Gender	Frequency	Percent
Female	200	51.4
Male	189	48.6
Total	**389**	**100.0**

Out of the total number of patients that were prescribed anti-malarial drugs within the three hospitals 51% were female while 49% were male.

Figure 2: Proportion of overall gender participation in the study.

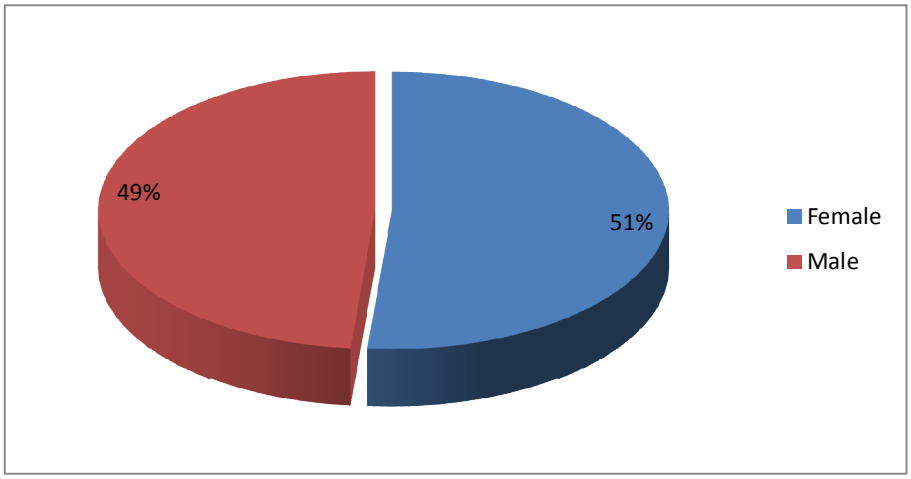

Table 3: Percentage of gender participation per hospital.

Hospital	Gender	Frequency	Percentage
MTRH	Female	44	47.83
	Male	48	52.17
	Total	92	100
Uasin Gishu	Female	110	54.46
	Male	92	45.54
	Total	202	100
Huruma	Female	46	48.42
	Male	49	51.58
	Total	95	100

Slightly more than half the number of patients prescribed Antimalarial drugs in Uasin Gishu hospital were females at 54.46% while in both MTRH and Huruma more males were prescribed Antimalarial drugs represented by 52.17% and 51.58% respectively.

Table 4: Overall Percentage of method of malaria diagnosis by the three hospitals.

Method of Malaria Diagnosis	Frequency	Percent
Laboratory	246	63.2
Clinical	143	36.8
Total	**389**	**100.0**

In terms of method of diagnosis used, Laboratory method accounted for 63% while clinical method accounted for 37% of all the diagnosis done during the study period.

Figure 2: Overall proportion of method of malaria diagnosis by the three hospitals.

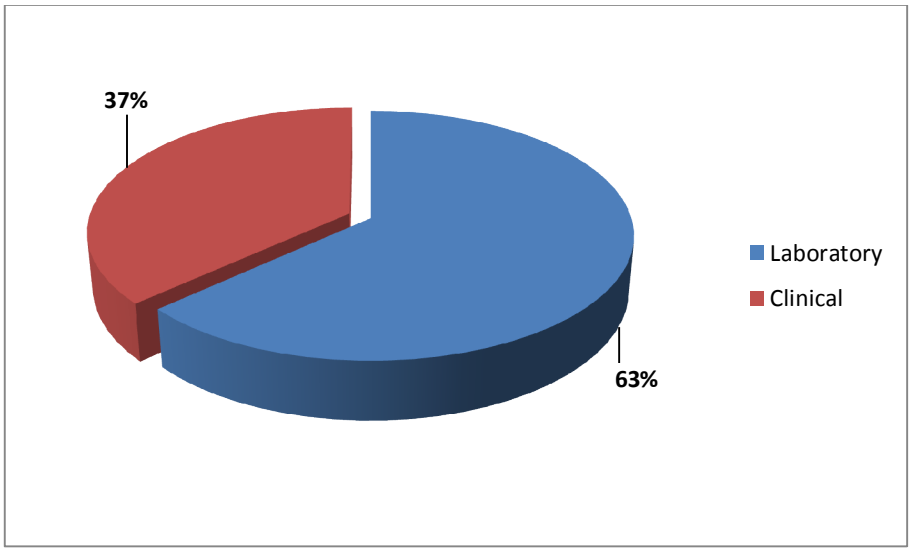

Table 5: Percentage of malaria diagnosis methods per hospital

HOSPITAL	Method of diagnosis	Frequency	Percentage
MTRH	Laboratory	46	50.00
	Clinical	46	50.00
	Total	92	100.00
Uasin Gishu	Laboratory	130	64.36
	Clinical	72	35.64
	Total	202	100.00
Huruma	Laboratory	70	73.68
	Clinical	25	26.32
	Total	95	100.00

Laboratory method of malaria diagnosis accounted for 73.68% in Huruma hospital and 64.36% in Uasin Gishu hospital while in MTRH laboratory and clinical diagnosis were equally conducted at 50% each.

Table 6: Overall percentage of laboratory methods used by the three hospitals.

Lab Method used	Frequency	Percent
Blood Smear	175	71.1
RDT	71	28.9

Total	389	100.0

For the Laboratory diagnosis done, blood smear method represented 71% while RDT represented 29%. None of the hospitals used polymerase chain reaction method.

Figure 3: Overall proportion of laboratory methods used by the three hospitals.

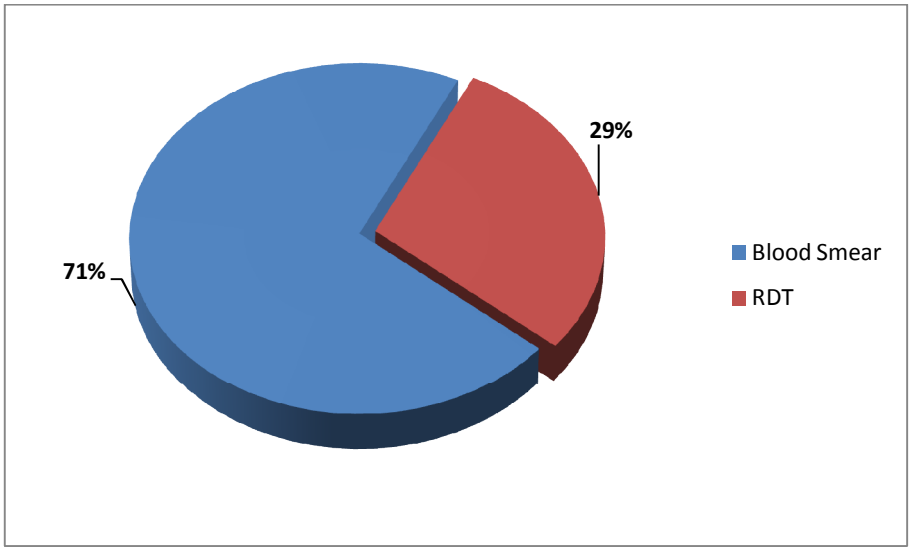

Table 7: Percentage of different laboratory methods used in each hospital.

Hospital	Lab Method Used	Frequency	Percentage
MTRH	Blood Smear	46	100
	Total	46	100
Uasin Gishu	Blood Smear	124	95.38
	RDT	6	4.62
	Total	130	100
Huruma	Blood Smear	5	7.14
	RDT	65	92.86
	Total	70	100

Blood smear accounted for all the lab tests done at MTRH, 95.38% for the tests done at Uasin Gishu and only 7.14% of the tests done at Huruma hospital.
RDT use was very high in Huruma hospital representing 92.86% of all the tests conducted during the study period.

Regarding the patients who had laboratory tests prior to receiving antimalarial agents:
17 out of the 46 tests done in MTRH were negative (i.e 37%).
36 out of the 130 tests done in Uasin-Gishu county hospital were negative (i.e. 28%).

9 out of the 70 tests done in Huruma county hospital were negative (i.e. 13%).
Thus, 25.2% of the patients who had laboratory tests prior to receiving antimalarial agents tested negative.

Figure 5: Overall number of participant in each special groups from the three hospitals.

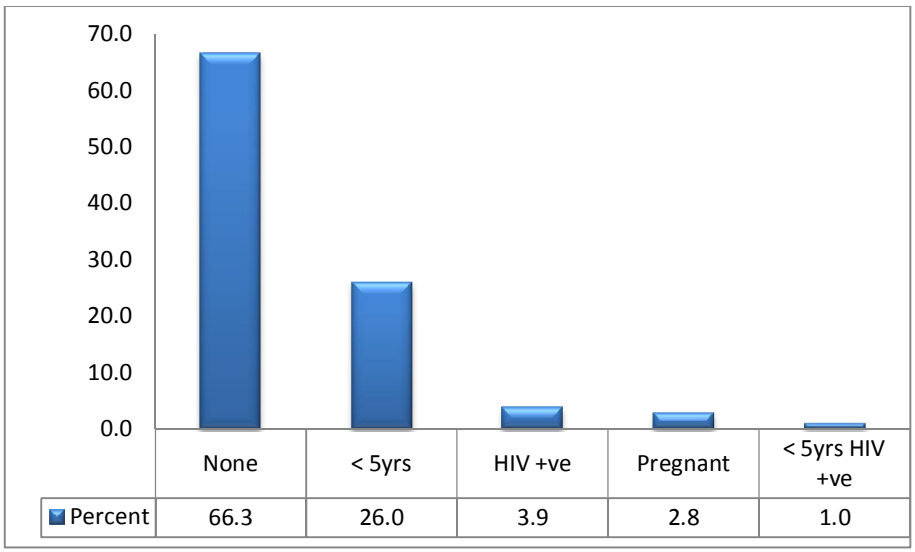

Table 2: Percentages of malaria diagnosis methods used in each special group.

Group	Method of diagnosis	Frequency	Percent
None	Laboratory	165	63.95
	Clinical	93	36.05
	Total	**258**	**100**
Pregnant	Laboratory	10	90.91
	Clinical	1	9.09
	Total	**11**	**100**
< 5Yrs	Laboratory	63	62.38
	Clinical	38	37.62
	Total	**101**	**100**
HIV+Ve	Laboratory	8	53.33
	Clinical	7	46.67
	Total	**15**	**100**
< 5yrs HIV +Ve	Laboratory	0	0.00
	Clinical	4	100
	Total	**4**	**100**

For pregnant women 90.9% of the diagnosis were done through laboratory tests while only 9.1% of the diagnosis was based on clinical signs.

For the under 5 years group, 62.4% of the diagnosis were done through laboratory tests while only 36.6% of them were done through clinical method.

53.3% of the diagnosis in the <5yrs and HIV+ve category were done through laboratory test while 46.7% of them were done using clinical method.

Table 9: Percentage of methods of malaria diagnosis in special groups per hospital

Special Group/Hospital	Method of diagnosis	Frequency	Percentage
MTRH			
None	Laboratory	33	50.00
	Clinical	33	50.00
	Total	**66**	**100.00**
Pregnant	Laboratory	2	66.67
	Clinical	1	33.33
	Total	**3**	**100.00**
< 5 Yrs	Laboratory	10	47.62
	Clinical	11	52.38
	Total	**21**	**100.00**
HIV+Ve	Laboratory	1	100.00
	Total	**1**	**100.00**
< 5yrs HIV+Ve	Clinical	1	100.00
	Total	**1**	**100.00**
Uasin Gishu			
None	Laboratory	81	62.31
	Clinical	49	37.69
	Total	**130**	**100.00**
Pregnant	Laboratory	6	100.00
	Total	**6**	**100.00**
< 5 Yrs	Laboratory	39	69.64
	Clinical	17	30.36
	Total	**56**	**100.00**
HIV+Ve	Laboratory	4	44.44
	Clinical	5	55.56
	Total	**9**	**100.00**
< 5yrs HIV+Ve	Clinical	1	100.00
	Total	**1**	**100.00**
Huruma			
None	Laboratory	51	82.26
	Clinical	11	17.74
	Total	**62**	**100.00**
Pregnant	Laboratory	2	100.00
	Total	**2**	**100.00**
< 5 Yrs	Laboratory	14	58.33
	Clinical	10	41.67

	Total	**24**	**100.00**
HIV+Ve	Laboratory	3	60.00
	Clinical	2	40.00
	Total	**5**	**100.00**
< 5yrs HIV+Ve	Clinical	2	100.00
	Total	**2**	**100.00**

Laboratory method of diagnosis accounted for 82.26% in Huruma, 62.31% in Uasin Gishu and 50% in MTRH for non-special group.

For the pregnant women category, laboratory method accounted for all the diagnosis conducted at Uasin Gishu and Huruma hospitals while in MTRH laboratory method accounted for 66.67%.

For <5yrs laboratory method accounted for 69.64% in Uasin Gishu and 58.33% in Huruma and 47.62% in MTRH.

Under the <5yrs HIV+ve category, clinical method accounted for all the diagnosis done in all the three hospitals.

Table 10: Overall results from laboratory method of diagnosis from the three hospitals.

Lab Results	Frequency	Percent
Malaria Positive	184	74.8
Malaria Negative	62	25.2
Total	**389**	**100.0**

Out of those patients prescribed for antimalarial agents, 75% of them had tested positive for malaria while 25% tested negative for peripheral parasitaemia. However, all of them were prescribed antimalarial drugs.

Figure 6: Overall results from laboratory method of diagnosis from the three hospitals

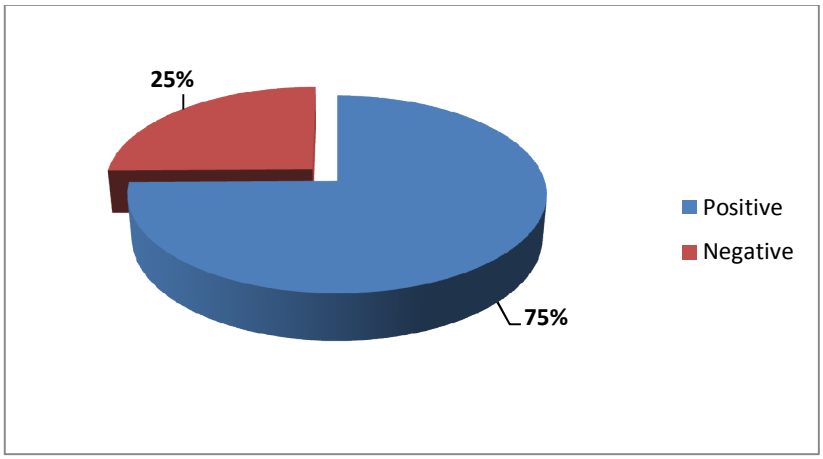

Table 11: Method of administration and the percentage of the Antimalarial prescribed

Method of administration	Antimalarial prescribed	Frequency	Percent
oral	AL	234	60.2
	DHAPQ	21	5.4
	Artequick(Artesunate/Mefloquine)	2	0.5
	Cortesiane Syrup	6	1.5
injections	Larither	7	1.8
	Quinine	4	1
	Artesunate	114	29.3
	Artemether	1	0.3
TOTAL		**389**	**100**

Orally given antimalarial drugs were AL, DHAPQ, Artequick and Coartesiane syrup. Antimalarial drugs given by injection were larither, quinine, artesunate and artemether.

Generally, AL was the most prescribed drug followed by artesunate injection.

Table 12: Percentage of Antimalarial prescribed per hospital

HOSPITAL	Antimalarial prescribed	Frequency	percentage
MTRH	AL	38	41.30
	Duocotexin	15	16.30
	Artequick	2	2.17
	Cortesiane Syrup	6	6.52
	Larither	4	4.35
	Quinine	3	3.26
	Artesunate	23	25.00
	Artemether	1	1.09
	Total	**92**	**100**
Uasin Gishu	AL	139	68.81
	Duocotexin	6	2.97
	Artesunate	57	28.22
	Total	**202**	**100**
Huruma	AL	57	60.00
	Larither	3	3.16
	Quinine	1	1.05
	Artesunate	34	35.79

	Total	**95**	**100**

Prescription of AL was high in Uasin Gishu and Huruma hospitals at 68.81% and 60% respectively while in MTRH it accounted for 41.30% of the prescriptions.
Duocotexin prescription accounted for 16.30% in MTRH and only 2.97% in Uasin Gishu but was not prescribed to any patient in Huruma hospital.
Prescription of Artesunate accounted for 25% in MTRH, 28.22% in Uasin Gishu and 35.79% in Huruma while on the other hand, Quinine prescription was low in both MTRH and Huruma hospitals represented by 3.26% and 1.05% respectively. No Quinine injection was prescribed to the patients in Uasin Gishu hospital.

Table 13: Percentage of Antimalarial prescribed in each special group per hospital

MTRH			
Special group/Hospital	**Antimalarial**	**Frequency**	**Percentage**
None	AL	31	46.97
	Duocotexin	10	15.15
	Artequick	2	3.03
	Cortesiane Syrup	2	3.03
	Larither	4	6.06
	Quinine	3	4.55
	Artesunate	14	21.21
	Total	66	100
Pregnant	AL	1	33.33
	Duocotexin	2	66.67
	Total	3	100
< 5 Yrs	AL	6	28.57
	Duocotexin	3	14.29
	Cortesiane Syrup	4	19.05
	Artesunate	8	38.1
	Total	21	100
HIV+Ve	Artemether	1	100
	Total	1	100
< 5yrs HIV+Ve	Artesunate	1	100
	Total	1	100

Huruma			
Special group/Hospital	**Antimalarial**	**Frequency**	**Percentage**
None	AL	35	56.45
	Larither	3	4.84
	Artesunate	24	38.71
	Total	62	100

Pregnant	AL	1	50
	Quinine	1	50
	Total	2	100
< 5 Yrs	AL	16	66.67
	Artesunate	8	33.33
	Total	24	100
HIV+Ve	AL	5	100
	Total	5	100
< 5yrs HIV+Ve	Artesunate	2	100
	Total	2	100

Uasin Gishu			
Special group/Hospital	**Antimalarial**	**Frequency**	**Percentage**
None	AL	95	73.08
	Duocotexin	6	4.62
	Artesunate	29	22.31
	Total	130	100
Pregnant	AL	5	83.33
	Artesunate	1	16.67
	Total	6	100
< 5 Yrs	AL	29	51.79
	Artesunate	27	48.21
	Total	56	100
HIV+Ve	AL	9	100
	Total	9	100
< 5yrs HIV+Ve	AL	1	100
	Total	1	100

Table 14. Antimalarial use in pregnancy.

Pregnant		
Antimalarial Prescribed	**Frequency**	**Percent**
AL	7	63.64
Duocotexin	2	18.18
Quinine	1	9.09
Artesunate	1	9.09
Total	**11**	**100**

Out of the 11 pregnant women who were prescribed Antimalarial drugs, 63.4% were prescribed AL, 18.2% of them were prescribed Duocotexin. All of them were in their first

trimesters. Quinine and Artesunate prescriptions represented 9.1% each and were all in their first trimesters too.

Other observations.

Prescriptions for out-patients with wrong dosages were corrected by the pharmacy staff during dispensing of the drugs to the patients.

Wrong dosages were mainly seen in antimalarials being given parenterally and were wrong in relation to weight of the patient and duration of use.

As noted in Table 12 above, Uasin Gishu County hospital, which has no in-patients, still had the highest number of Artesunate injection prescribed since many patients were initiated in Artesunate injection before continuing with oral drugs.

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS.

From the results, only 63% of those prescribed for antimalarial agents during the entire study period had prior malaria diagnosed by laboratory method and 25.2 % of them had tested negative yet they were still given antimalarial drugs. Therefore, still a large percentage (37%) of patients who were given antimalarial drugs were diagnosed clinically. Moreover, 25.2% of the 63% who had laboratory test were negative for malaria yet were still given anti-malarial drugs. This clearly shows some clinicians disregard laboratory results. Such has also been reported in Afghanistan, which has a much lower incidence of malaria than Africa, yet fever has substantially been misdiagnosed as malaria in most cases mainly due to false positive laboratory diagnoses of malaria and the clinicianséô disregard of negative slides results. (Leslie *et al*. 2012).

Most prescribers chose to diagnose malaria clinically because they felt some patients had very clear malaria symptoms, the patients were from malaria endemic region thus must have had contacted malaria based on their symptoms, felt that laboratory diagnosis would take too long yet the patient was suffering or/and had little faith in laboratory results. The danger of misdiagnosing malaria in patients with febrile illness is that the patient ends up not being treated for the right condition i.e. the actual cause of febrile illness is left unattended (Reyburn *et al.* 2004). In fact, symptomatic diagnosis of malaria overestimates its actual prevalence while underestimating the prevalence of other conditions in children (Choge *et al*. 2014).

Laboratory diagnosis method was highest in pregnant women (90%) probably because of the general awareness that drugs in pregnant women must be used when it is absolutely necessary.

Uasin Gishu county hospital and MTRH had the highest percentages of blood smear method (95% and 100% respectively) and it was because most laboratory technicians believe RDTs

are associated with many false results. However, Huruma county hospital had 93% usage of RDTs and was because the laboratory staff believed that RDTs are faster and more modern.

In regard to the antimalarials prescribed, AL was the most commonly prescribed antimalarial agent. This is because, majority of the malaria cases were uncomplicated and AL is the recommended first line. The efficacy of AL and DHAPQ are almost equal in management of uncomplicated *P. Falciparum.* (Bousema *et al*, 2013 and Agarwal *et al*, 2013). This explains why some prescribers recommended DHAPQ over AL and also, unlike AL, it requires once daily dose hence compliance is almost guaranteed. However, in uncomplicated malaria, AL is much superior to quinine and has less side effects and dosing frequencies too compared to quinine (Achan *et al*. 2009).

Severe complicated malaria is treated using artesunate, However, many patients were initiated on Artesunate injection before continuing with oral drugs (AL) especially in Uasin Gishu and Huruma county hospitals. Although few cases of severe complicated malaria were managed using Larither (Artemether) injections, artesunate is the treatment of choice for severe falciparum malaria worldwide (Arjen *et al*. 2010).

The four patients who were given quinine were all pregnant mothers in their first trimester and this is the drug of choice in managing severe malaria during the first trimester. This is in tandem with the fact that usage of right antimalarial drugs greatly reduces the malaria complications in pregnancies e.g. miscarriages (McGready *et al*. 2012).

DHAPQ use was mainly in MTRH since the drug is easily available there. The patients from Uasin Gishu who had been prescribed the same had to get them from private pharmacies or chemists in town. The use of DHAPQ is justifiable because its efficacy is comparable to that of AL hence a valid option for the treatment of uncomplicated *P. falciparum* malaria (DôAllesandro *et al*, 2011).

Artequick (Artemisinin/Piperaquine) and Coartesiane (AL) syrup were only found and prescribed in MTRH.

Prescriptions for out-patients with wrong dosages were corrected by the pharmacy staff during dispensing of the drugs.

Wrong dosages were mainly seen in antimalarials being given parenterally and were wrong in relation to weight of the patient and duration of use.

Conclusion:

In as much as laboratory method is the recommended criteria of malaria diagnosis, many prescribers still diagnose malaria clinically, which is against the national guidelines that states malaria is only diagnosed by presence of peripheral parasitaemia. Thus a shift from presumptive treatment to laboratory confirmed diagnosis and treatment in all areas, regardless of age and level of malaria transmission is needed and this is feasable due to RDTs (DôAcremont *et al.* 2009).

According to the national guidelines, the first line treatment of uncomplicated malaria should be AL. Severe complicated malaria should be managed using artesunate injection. Furthermore, artesunate should be changed to AL once the patient is able to take oral medications. However, Artesunate is being prescribed as a start dose in many uncomplicated malaria episodes, which is wrong. Therefore, efforts and stratergies are needed to contain the emergence of artemesinin-resistant malaria (Aung *et al,* 2012).

Use of antimalarial agents in pregnancy conformed to the national guidelines i.e. artesunate was never given in the first trimester.

DHAPQ is the second line for uncomplicated malaria but all those who were prescribed the same had no evidence of treatment failure by AL.

Therefore, the national guidelines on malaria treatment are not being fully followed in the major Uasin Gishu county hospitals and MTRH.

Recommendations.

There is a need to sensitize all health workers, especially the prescribers, on importance of laboratory confirmation of malaria and the antimalarial drugs to be used in relation to the

national guidelines. Therefore, continous medical edication, workshops and seminars on the same are highly recommeded to provide refresher courses to health workers. Futher more, standardization of laboratories in the hospitals to get credible results and monitoring of antimalarial usage will go a long way in implementing the national guidelines on malaria management.

Information dissemination plan

The findings of this research will be taken to the Chief Officer of Health, Uasin-Gishu county. Through his office, the above recommendations can be disseminated to all health facilities in the county.

For MTRH, copy of this research shall be deposited at Monitoring and Efficiency department as part of the requirement by the hospital, then the dissemination of the information passed down all the clinical services department through the office of the Deputy Director in-charge of Clinical Services.

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APPENDIX I

ANTIMALARIAL USE IN MAJOR PUBLIC HOSPITALS IN ELDORET TOWN: REVIEW OF USE IN UASIN GISHU AND HURUMA COUNTY HOSPITALS AND MTRH.

DATA COLLECTION FORM

SECTION ONE: BIO-DATA

1: a) Patient Hospital Numberé é é é é é é é é é é é é é ..

b) Gender Male [ ] Female [ ]

c) Ageé é é é é é é é é é é é é é

d) Weight.....

e) Residence.....

SECTION TWO

2: a) Method of malaria diagnosis used

[ ] Laboratory diagnosis

[ ] Clinical diagnosis

b) Laboratory method, if used for diagnosis

[ ] Polymerase Chain Reaction

[ ] Blood Smears

[ ] Rapid Diagnostic Test

[ ] Other (Specify).....

c) Special group of patients

[ ] None

[ ] Pregnant

[ ] Under 5 years

[ ] HIV positive

d) i: Co-morbidity if anyé .....

ii: Management of the co-morbidity if any.....

.....

e) i: Antimalarial prescribedé é é é é é é é é é é é é é é é é é

ii: Route of administrationé é é é é é é é é é é é é é é é é é

iii: Dosage and duration of therapyé é é é é é é é é é é é é é é