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RESEARCH ARTICLE

A PROMISING TREND IN COMBATING MALARIA: A CASE STUDY IN ERITREA, EAST AFRICA.

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Abstract

Malaria is one of the most public health problems in Eritrea with 67% of the population living in areas at risk. In Eritrea, three hospitals were selected from the three Zobas considered being at significant malaria risk. Blood samples were collected from the patients suffer from malaria disease and the samples were diagnosis using giemsa staining. After conformation and identify the parasitic species, the patients were treated with the first line treatment of uncomplicated falciparum malaria is Artesunate + Amodiaquine (AS + AQ). The second line treatment for treatment failures is oral Quinine. The treatment for severe malaria is parenteral Quinine. Treatment of malaria during pregnancy is Quinine. The objective of this study was to assess the therapeutic efficacy of the antimalarial drug regimen adopted since 2007 in the country. The drugs were administered following the routine clinical treatment and protocols of the hospitals. All patients who were admitted or visited the hospitals with malaria cases during the study period were included. There were a total of 131 malaria related cases observed in the three hospitals. Adequlla Hospital accounts 24.4 %, (32) Keren Hospital 23.6 % (31) and Gash Barka Referral Hospital 52.0 % (68). Out of the total 131 malaria cases 26.7% (35) were females and 73.3 (96) were males. In terms of age groups patients in the age group 0-5 accounts 3% (4), age group 6-20 37% (48), and age group >20 60% (79). During the study period there was no treatment failure observed in the three hospitals, all treated patients either with Artesunate + Amodiaquine or/and Quinine showed positive response as it was confirmed by microscopic diagnosis and clinical observation. This finding, as a baseline report envisages further assessment and monitoring activities all over the country.

Introduction:-

Malaria, a devastating disease is a public health threat in many areas of the world, malarious areas and especially sub-Saharan Africa (Mandal *et al.*, 2011). It is the leading causes of morbidity and mortality. Majority of the deaths are children under the age of five and pregnant women attributed to their immature and weakened immunity respectively (Peter, 2011). Protozoa of the genus Plasmodium cause malaria and four species are responsible for the disease in humans. *Plasmodium. falciparum* causes the most severe disease (Zhong *et al*., 2008). Malaria is spread to humans by the bite of female mosquitoes of the genus *Anopheles* but transmission by inoculation of infected blood and through congenital routes is also seen (Teka *et al*., 2008). These mosquitoes feed at night and their breeding sites are primarily in rural areas. In all types of malaria, the periodic febrile response (fever) is caused by rupture of mature schizonts. In *P. Vivax* and *P. Ovale* malaria fever occurs every 48 hours, whereas in *P. malariae*, maturation occurs every 72 hours. In *P. falciparum* malaria fever may occur every 48 hours, but is usually irregular, showing no distinct periodicity (MoH, 2008).

Malaria is one of the most public health problems in Eritrea with 67% of the population living in areas at risk for the disease. Malaria accounts for 30% outpatient morbidity, 28% of all hospital admissions, and 7.4% of deaths of hospitalized children aged less than five years. In Eritrea the main malaria parasite is *P. falciparum* followed by *Plasmodium vivax* (Mandal *et al.*, 2011). Eritrea is a semi-arid tropical country, situated in the horn of Africa and lies approximately between Latitude 12º42' N, 18º2'N and Longitude 16º30'E and 43º20'E. It has an area of ~124,000 sq. kms, including the Dahlak Archipelago and the islands in the Red Sea, with altitudes that range from below sea level to 3,000 meters above sea level country-wide (Sintasath *et al.*, 2005). The country is divided into six administrative regions (*Zobas*). Four of the Zobas are considered to be at significant malaria risk, with the highest risk Zobas being Debub and Gash Barka and the lowest risk Zoba is the Northern Red Sea (Yukich *et al.*, 2009; Ceccato *et al*., 2007; Graves *et al.*, 2003). Transmission of malaria is usually described as highly seasonal and unstable, although this generalization masks a high variability (Nyarango *et al*., 2006).

The Government of Eritrea and the Ministry of Health intensively working hard to reduce the incidence, prevalence and death due to malaria through integrated malaria control and management strategies. The efforts made so far were so successful in that both the overall mortality and morbidity have been reduced. However, there is concern that the development of resistance to alternative antimalarial reported elsewhere (Mita and Tanabe, 2012) could also be revealed in Eritrea. Currently morbidity and mortality due to malaria are down by over 90 % (Asmelash, 2013). There could be so many factors that contributed to the dramatic reduction in malaria morbidity and mortality in the country. Some of the main contributory factors given for an overall reduction of the malaria burden during the last twenty years could be: Commitment and dedication of the Government and Ministry of Health (MoH, 2005), increased community awareness and participation in environmental vector control, effective planning and implementation of programs, followed by continuous supervision, regular monitoring and evaluation, improvement in early diagnosis and timely case management, the use of combination therapy such as chloroquine (CQ) + sulfadoxine-pyrimethamine (SP) in 2002 and Artesunate + Amodiaquine in 2007 as first line drug, high ITN (insecticide treated net) coverage, high re-impregnation rate and high utilization of nets, effective and functional partnership of country with partners to get both technical and financial support and shorter rainy seasons (MoH, 2005; Carneiro *et al*., 2012; Asmelash, 2013).

The key to effective management is early recognition, assessment, and appropriate antimalarial and supportive therapy. Efficient drug treatment involves targeting of an essential and critical biological process in the malaria parasite. Incidentally, *Plasmodium* parasite is highly adapted to its unique environments and many genes show little or no sequence similarity to other genes encoding characterized proteins (Mwangi and Ranford-Cartwright, 2013). Artemisinin-based combination therapy (ACT) is now the treatment of choice for uncomplicated *Plasmodium falciparum* malaria. Currently, the following four forms of ACT are recommended by the World Health Organization (WHO) artemether and lumefantrine(AL), artesunate and amodiaquine (AS&AQ), artesunate and mefloquine(AS+MQ) and artesunate and sulphadoxine-pyrimethamine (AS+SP) (Mihreteab *et al*., 2014). In Eritrea, the first line treatment of uncomplicated *falciparum* malaria is Artesunate + Amodiaquine (AS + AQ). The second line treatment for treatment failures is oral Quinine. The treatment for severe malaria is parenteral Quinine. Treatment of malaria during pregnancy is Quinine (MoH, 2008). The overall objective of treating uncomplicated malaria is to cure the infection. This is important as it will help prevent progression to severe disease and prevent additional morbidity associated with treatment failure. The primary objective of antimalarial treatment in severe malaria is to prevent death**.** Prevention of recrudescence and avoidance of minor adverse effects are secondary.

Objective:-

The objective of this study was to assess the therapeutic efficacy of the different antimalarial drug used for the treatment of uncomplicated *Plasmodium* species in Eritrea. The study was also attempted to oversee the malarial situation of the country by selected three hospitals which are located in the malariuos areas of the country. Therefore, it is important to closely monitor any development of resistance to the current drug regimens of the country. To realize the objectives of the present study the following experiments or investigations were carried out. To collect the blood sample from patients suffer from malaria disease, and the samples were diagnosed using giemsa staining. After conformation and identify the parasitic species, the patients were treated with the first line drug Artesunate + Amodiaquine (AS+ AQ mixed), the second line dug Quinine only recommended the patients who diagnosed to be in severe malaria and those with mixed *Plasmodium* species with P. *falciparum* and *P. vivax.*

Materials and methods:-

Study sites:-

To realize the objectives of the present study the following experiments or investigations were carried out by three hospitals were selected from the three Zobas considered being at significant malaria risk. The hospitals are Adiqualla Hospital in Zoba Debub, Keren Hospital in Zoba Anseba, and Gash Barka Referral Hospital, Barentu in Zoba Gash Barka.

Study period:-

The study period of the three hospitals was determined based on the previous malaria history obtained from the hospitals and the existed rainy season of the areas. As a result the study time range selected for Adiqualla Hospital was from July 1 to August 31, Keren Hospital from July 16 to September 15, and Gash Barka Referral Hospital from August 15 to October 1, 2014. During the study period, about two months, information about the prevalence of malaria and drug resistance in the areas, concerning the clinical efficacy of combination therapies introduced by the Ministry of Health, Eritrea, are gathered. The research project was designed following the research guideline prepared by National Commission for Higher Education (NCHE) and the ethical issues are considered. The human subject protocol involved was approved by Eritrean Institute of Technology and NCHE. All patients who admitted or visited the hospital with malaria cases during the study period are included. The drugs were administered following the routine clinical treatment and protocols of the hospitals. Malaria patients were treated according to body weight under direct observation. At each hospital, medical history and *case history* of each patient, including personal data, frequency of malaria attacks, and use of anti-malarial drugs is recorded in table 1.

Collection of blood sample:-

Blood samples were collected from patients with malaria disease. The blood specimen must be taken before commencement of malaria therapy, Blood samples should be collected between 11 a.m. and 1 p.m. Thick blood smears are typically used as a screening tool, and thin blood smears are used to observe detailed parasite morphology.

Giemsa staining technique:-

(Emanul Goldman and Lorrence Green, 2009)

Thin blood smears are separately made on a clean glass slide and heat fixed. Then the blood film are treated with 100% methanol for 1 minute and then air dry the slides followed by flooding with working giemsa solution stain for 10 to 60 minutes. Then the slide was washed in tap water or in phosphate buffer. Wipe the stain off the bottom of the slide, air dry and then examined under oil immersion lens of a compound light microscope.

Chemotherapy:-

All patients who admitted or visited the hospital with malaria cases during the study period are included. Malaria patients were treated according to body weight under direct observation. At each hospital, medical history and *case history* of each patient, including personal data, frequency of malaria attacks, and use of anti-malarial drugs is recorded. Majority of the patients were treated with the first line drug (AS 100mg + AQ 200mg mixed) and Quinine 300mg by direct observed treatment (DOT) and observe the patient for around 30 minutes. Emphasize that all doses must be taken for 3 days, even if patient feels better after the first or second dose. If vomiting occurs within 30 minutes after drugs administration repeat the dose.

When treatment with first line drug (AS + AQ) of therapy has failed (if signs and symptoms of malaria do not subside after taking full dose), another first line antimalarial drug i.e Quinine 300mg should be utilized. The drug of choice is oral Quinine given at a dose of three times administered for seven days. Some patients who were diagnosed to be in severe malaria and those with mixed *Plasmodium* species, with *P. falciparum* and *P. vivax*, were treated with the second line drug Quinine 300mg as required. The drug of choice is oral Quinine given at a dose of three times administered for seven days (Fig 1). For children below 4 kg, the dosage is 10mg/kg body weight given three-times a day for 7 days. The quinine tablets can thus be reconstituted into syrup based on the weight of the patient.

Results and discussion:-

All patients who admitted or visited the hospital with malaria cases during the study period were included. There were a total of 131 malaria related cases observed in the three hospitals, distributed by zoba as indicated in table 1.

Adequlla hospital accounts 24.4 %, (32) Keren hospital 23.6 % (31) and Gash Barka Referral hospital 52.0 % (68). As it was expected Gash Barka referral hospital had more cases than the other two hospitals. Out of the total 131 malaria cases 26.7% (35) were females and 73.3 (96) were males. In term of age groups patients in the age group 0-5 accounts 3% (4), age group 6-20 37% (48), and age group >20 60% (79). Severe malaria can occur in the absence of fever. Therefore, in all patients with suspected severe malaria with fever or without fever or history of fever, immediately parasitological diagnosis should be done.

The laboratory diagnostic of malaria is made by microscopic examination of a giemsa stained thin smear of peripheral blood examine under oil immersion objective lens of a compound light microscope, the protozoa can be detected growing in the RBCs the *Plasmodium* infected erythrocytes in blood smears are slightly enlarged, the feeding protozoan resembles a ring shaped trophozoites within the RBCs, the diagnostic features was investigated by Moselio Schaechter, 1993; Garcia, 2006 and Forbes *et al.,* 2007. Typically all sizes of red blood cells are infected. Often 5% or more of the circulating erythrocytes are infected Heelan, and Ingersoll, 2002; Leventhal, and Cheadle, 2002. Multiple ring forms can be seen in a single red blood cell Woods, and Walker, 1996. Multiple smears may be needed before the diagnosis is confirmed (Christopher Grace, 2003). As it was expected the main malaria parasite observed was *P. falciparum* followed by *P. vivax* as discrided by Mandal *et al*., 2011. The *P. falciparum* accounts 67.18% and *P. vivax* accounts 32.82% of the total observed malaria cases. But the malarial species distribution in the country seems to be affected depend on the environmental condition present in the high and low land. In the high land, Adiqualla the *P vivax* cases were more than the *P. falciparum* cases, whereas the *P. vivax* cases in the low lands, keren and Gash Barka were very low (Fig 2).

During the study period there were no treatment failure in the three hospitals, all treated patients either with Artesunate + Amodiaquine or/and Quinine showed positive response as it was confirmed by microscopic diagnosis and clinical observation. This finding, even if it covers only three hospitals, is very encouraging and in agreement with the reports given by other researchers (MoH, 2005; Carneiro *et al*., 2012; Asmelash, 2013). The assessment made on the therapeutic efficacy of Artesunate and amodiaquine in five most malarious sites of Gash Bark by Mihreteab *et al.,* (2014) indicated that therapeutic efficacy of AS + AQ meets WHO efficacy criteria for continue use of ACTs against *P. falciparum* infections.

However in the same study treatment failure has occurred in Goluji subzone which borders the Sudan and Ethiopia. This condition warrants for continues efficacy monitoring of the current malaria treatment regimen. The current commitment and dedication of the Government and Ministry of Health (MoH) in increasing community awareness and participation in environmental vector control, effective planning and implementation of programs, followed by continuous supervision, regular monitoring and evaluation, improvement in early diagnosis and timely case management are the milestone of the observed dramatic reduction in malaria morbidity and mortality in the country. The artesunate based first line treatment has been used at all levels of the health facilities since 2007. Continues assessment and monitoring of the therapeutic efficacy of the current regimen for malaria is appropriate and mandatory as there is always a concern that the development of resistance to antimalarial drugs reported elsewhere (Mita and Tanabe, 2012) could also be revealed in Eritrea.

Conclusion:-

The malarial situation of the country seems to be in good condition as it was described by different researcher's morbidity and mortality due to malaria are down. The Artesunate based first line treatment has been used at all levels of the health facilities since 2007. This finding, as a baseline report envisages further assessment and monitoring activities all over the country. In this study there were eight non-responding patients for the AS + AQ treatment but the same patients were responded to the second line treatment, Quinine. Therefore, in this study there was no treatment failure observed. The need of continues monitoring strategy is with the idea that within a geographical area malaria infections demonstrate a range of drug susceptibility. Over time, resistance becomes established in the population and can be very stable; persisting even long after specific drug pressure is removed.

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Table 1. Malaria cases observed in the three hospitals

S.no	Hospitals name	Age & Gender								Total
		0-5 years		6-20 years		Above 20 years		Total		
		F	M	F	M	F	M	F	M	
1	Adiqualla Hospital	0	1	1	13	9	8	10	22	32
2	Keren Hospital	0	0	1	6	4	20	5	26	31
3	Gash Barka Referral Hospital	1	2	9	18	10	28	20	48	68
	Grand Total									**131**

Figure 1. Chemotherapy

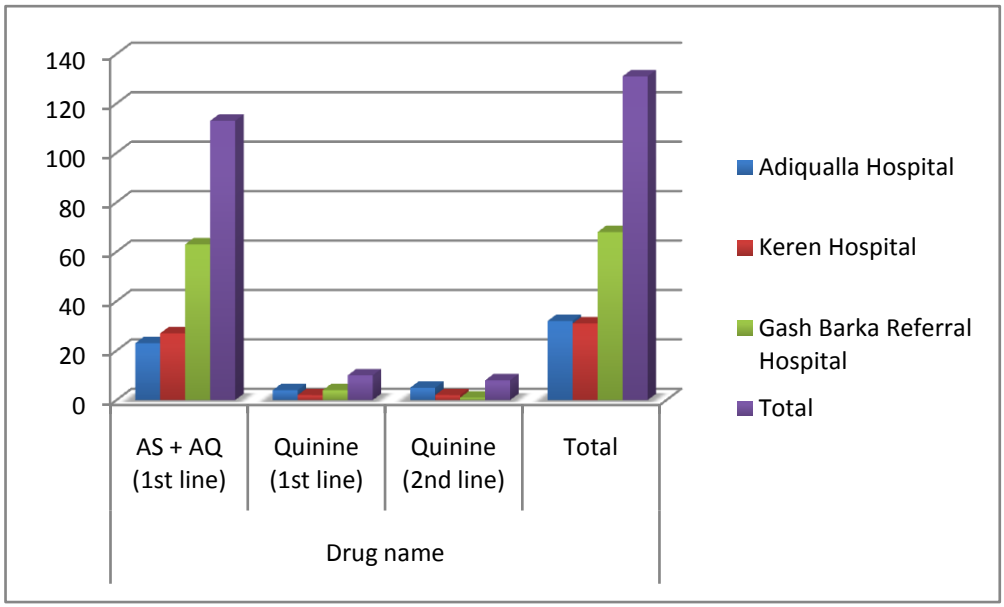
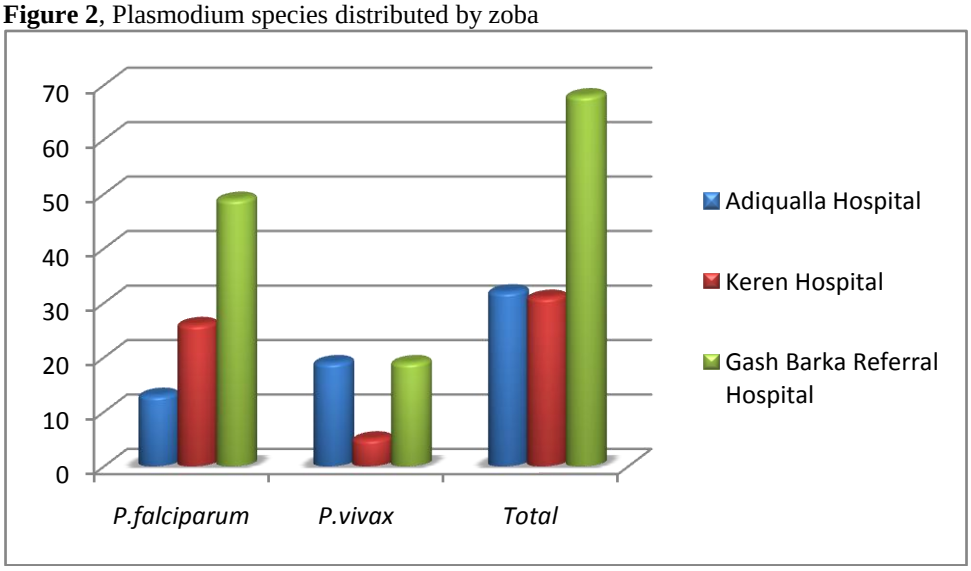


Figure 2, Plasmodium species distributed by zoba



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