IDENTIFICATION OF BARRIERS TO EFFECTIVE TREATMENT AND PREVENTION OF MALARIA IN KHARTOUM, SUDAN

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by

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ABSTRAK

Malaria merupakan salah satu dari penyebab kematian yang utama di Sudan. Prevalens yang tertinggi adalah dalam kalangan wanita mengandung dan kanak kanak. Kematian dianggarkan sekitar 3500 kes setiap tahun. Hampir 13 peratus kemasukkan ke hospital adalah akibat dari malaria. Walaupun terdapat kemajuan Program Pengawalan Malaria diperingkat Nasional di Sudan, sasaran mengenai pembasmian dan penghapusannya tidak tercapai. Kajian semasa dijalankan untuk mengenal pasti halangan untuk pencegahan dan rawatan berkesan malaria di Sudan. Kajian ini dijalankan di negeri Khartoum. Satu kajian keratan rentas telah dijalankan untuk menilai amalan ahli farmasi komuniti dalam pencegahan dan rawatan malaria. Orang ramai di Khartoum juga dinilai untuk pengetahuan malaria mereka selain daripada amalan pencegahan dan rawatan mereka. Rawatan malaria di hospital awam juga dinilai secara retrospektif dan prospektif. Keputusan menunjukkan bahawa ahli farmasi komuniti tidak mempunyai pengetahuan malaria dan amalan rawatan malaria yang mencukupi. Lebih kurang 66.2% dari ahli farmasi komuniti yang di selidiki mempunyai skor pengetahuan kurang dari 50%. Terdapat hubungan yang signifikan antara skor pengetahuan ahli farmasi dan menjalani latihan untuk pencegahan dan rawatan malaria (P-value 0.008). Kajian itu mendedahkan laporan kesan advers (ADRs) ubat-ubatan antimalarial yang rendah oleh ahli farmasi komuniti. Ahli farmasi komuniti melaporkan kekurangan pengetahuan, kekurangan latihan dan masa sebagai penghalang utama dalam pencegahan dan rawatan malaria serta aktiviti pelaporan kesan advers. Orang ramai di Khartoum menunjukkan pengetahuan yang baik

mengenai gejala malaria, komplikasi dan ubat-ubatan. Lebih kurang 86.9% daripada mereka menyatakan gigitan nyamuk merupakan penyebab utama berlakunya malaria. Demam dan sakit kepala merupakan simptom malaria yang kerap dilaporkan iaitu 84.2% and 74.4% masing masing dalam kalangan orang ramai yang di kaji. Walaupun mereka mempunyai pengetahuan yang baik mengenai kaedah pencegahan, namun masih kurang digunakan dalam kalangan masyarakat. Lebih dari suku (28.9%) dalam kalangan mereka tidak menggunakan kaedah pencegahan malaria.Amalan diagnosis dan rawatan kendiri telah dilaporkan dalam kalangan orang ramai. Penilaian rawatan malaria di hospital awam menunjukkan ketidakpatuhan dalam banyak aspek. Diagnosis klinikal dan rawatan secara andaian masih berlaku dalam amalan walaupun terdapat kemudahan penyiasatan makmal. Dos ubat dan tempoh rawatan yang kurang sesuai juga dilaporkan. Laporan mengenai masalah ubat-ubatan antimalarial yang rendahjuga turut di dapati dalam amalan. Secara umumnya amalan rawatan malaria yang tidak sesuai dalam kalangan farmasi komuniti, masyarakat dan hospital awam, tingkah laku penggunaan ubat ubatan yang tidak sesuai dan tidak menggunakan kaeadah pencegahan yang sesuai oleh komuniti boleh menjadi halangan dalam cara pembasmian malaria di Sudan.

IDENTIFICATION OF BARRIERS TO EFFECTIVE TREATMENT AND PREVENTION OF MALARIA IN KHARTOUM, SUDAN

ABSTRACT

Malaria is one of the main causes of death in Sudan. The highest prevalence is among children and pregnant women. The estimated deaths were 3500 cases per year. Near thirteen percent of the hospital admissions were due to malaria. Despite the achievements of the National Malaria Control Programme in Sudan, still the targets on eradication and elimination were not reached. The current research was carried to identify the barriers to effective prevention and treatment of malaria in Sudan. The research was conducted in Khartoum state. A prospective cross-sectional survey was carried to assess the community pharmacist's practices of malaria prevention and treatment. The public in Khartoum were also assessed for their malaria knowledge in addition to their prevention and treatment practices. Malaria treatment in a public hospital was also investigated retrospectively and prospectively. The results showed that community pharmacists had inadequate malaria knowledge and malaria treatment practices. About 66.2% of the surveyed community pharmacists had less than 50% knowledge score. There was significant relationship between pharmacist knowledge score and receiving training on malaria prevention and treatment (P-value 0.008). The research revealed under reporting of antimalarial adverse drug reactions (ADRs) by the community pharmacists. The community pharmacists reported lack of knowledge, lack of training and time as main barriers to their effective contribution in malaria prevention and treatment and ADRs reporting activities. The publics in Khartoum showed good knowledge regarding malaria symptoms, complications and drugs. About 86.9% mentioned mosquitos' bites as the main cause of malaria. Fever and

headache as malaria symptoms were reported by 84.2% and 74.4% of the surveyed publics. Although they had good knowledge about prevention methods, but still under used by the community. More than one quarter (28.9%) were not using malaria prevention methods. The practices of self-diagnosis and self- treatment were reported among the publics. Assessment of malaria treatment in a public hospital setting revealed inappropriateness in many aspects. Clinical diagnosis and presumptive treatment were still in the practice despite availability of laboratory investigation facilities. In appropriate drugs dosing and duration of treatment were also reported. Under reporting of antimalarial drugs related problems was also in the practice. Generally inappropriate malaria treatment practices in community pharmacies and public hospital, inappropriate drug use behavior among the community and under use of prevention methods by the community were identified as obstacles in the way to malaria eradication in Sudan.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Malaria is a parasitic life threatening disease .The main malaria vector is the infected female of Anopheles mosquitos. Malaria caused mainly by the parasite Plasmodium. The most identified plasmodium species are Plasmodium Falciparum, Plasmodium Vivax, Plasmodium Malariae, Plasmodium Oval and Plasmodium Knowlesi. Plasmodium Falciparum is the dominant specie in Africa and it is responsible of the most global malaria mortalities. Plasmodium Vivax is found in many countries outside Sub-Saharan Africa. Ninety percent of malaria cases and 92% of malaria deaths were from Sub-Saharan African countries. Seventy percent of malaria deaths were among children under five years of age (World Health Organization, 2017).

In the last few years, there was an obvious increase in efforts and funding to control the disease, especially by the Global Fund to Fight AIDS, Tuberculosis and Malaria and World Health Organization (WHO). In WHO malaria report 2016 the fund of malaria control and elimination was increased by US$ 0.06 billion since 2010. Many countries like United States of America, United Kingdom, Germany, Japan and Canada are contributing to this fund. The governments of the endemic countries contribute by about 32% of funding. This contribution will be a burden on endemic countries economics since the majority are developing countries (World Health Organization, 2017).

The great achievements in controlling malaria appeared in many aspects. The number of malaria-endemic countries reduced to 90 countries compared to 108 in 2000 without any re-establishment of malaria in any of the malaria-free countries since

2000. In 2015 10 countries had less than 150 indigenous cases and 9 countries had between 150-100 cases. Elimination of malaria from another 10 countries by 2020 is of the objectives of the Global Technical Strategy for Malaria 2016-2030 (World Health Organization, 2017).

Increased coverage of malaria interventions between 2010 -2015 was reported. About 57% of the Sub-Saharan African populations benefited from indoor residual spraying (IRS) and insecticides treated nets (ITNs) as vector control methods. Use of intermittent preventive therapy (IPT) for malaria prevention during pregnancy was increased by 31%.

Worldwide the malaria case incidence rates decreased by 40% between 2000-2015 (21% between 2010 -2015). The mortality rates also decreased by 62% between 2000-2015 (29% between 2010-2015). The decrease in mortality has led to an increase in the life expectancy at birth by 1.2 years in the WHO African region (World Health Organization, 2017).

The WHO report also showed an increase in the access to more than fifty percent of the suspected cases in the African region to diagnostic testing and treatment at public health facilities. However, the constraints of under-resourced health systems and poor accessibility of most of the populations at risk to services are still there. The progress in malaria control is threatened by insecticides resistance and antimalarial drugs resistance (World Health Organization, 2017).

1.2 Malaria in Sudan

Sudan is an African country with 39 million population in 2016 (World Health Organization, 2016). It is classified by WHO in the Eastern Mediterranean region. According to World Bank income classification, it is lower to middle-income country.

Malaria is a real health problem in Sudan. The real burden of malaria in Sudan was underestimated as most of the reported data came only from the public hospitals and public health centers (Abdalla, Malik, & Ali, 2007).

People of low socioeconomic status and those who live in rural areas were the most affected. Still there are many problems associated with malaria diagnosis and treatment in Sudan. According to the last malaria indicator survey in Sudan majority of the people seek malaria treatment at public facilities. In public facilities malaria treatment was supposed to be provided free of charge, however; it was not the case people have to pay for the treatment. Inappropriate diagnosis and treatment were in the practice. Use of Monotherapy in form of Artemether injection was very high in public facilities. The highest use of monotherapy was reported in Khartoum state. Malaria in pregnancy and anemia as malaria complication were also of malaria-related problems. Anemia mostly affects pregnant women and children less than five years of age. Regarding malaria prevention still, the ownership of ITNs was low (1.4-1.8 net per household). Availability and use of other preventive methods were also less than the required. The public information on malaria was mainly obtained from the media and the sources of information vary from one state to another (Federal Ministry of Health, 2017a).

1.2.1 Epidemiology of malaria in Sudan

Malaria remains one of the main causes of deaths in Sudan with a higher incidence among children, refugees and internally displaced people. Malaria indicator survey 2016 showed that malaria prevalence was 5.9% with higher prevalence among Children, males and pregnant females. About 12.2% of hospital admissions are due to malaria (Federal Ministry of Health, 2017a).

In 2015 the major Plasmodium species found in Sudan were *P. falciparum and P. vivax* which accounted for 95% and 5% respectively. According to malaria indicator survey 2016, the *Plasmodium falciparum* was 87.6% and the *Plasmodium vivax* was increased to 8.1%, while the mixed infection was 4.3%. *P.vivax* infection alone or mixed infection was more prevalent in Darfur, Khartoum and River Nile states. The prevalence of malaria in urban and rural areas differs among different states (Federal Ministry of Health, 2017a).

The major Anopheles species (the vector) in Sudan are *Anopheles arabiensis, Anopheles funestus, Anopheles gambiae, Anopheles nili,* and *Anopheles pharoensis*. In the last updated WHO report 2015, the reported confirmed malaria cases in Sudan were 586,827 while the estimated cases were 1,4 million cases. The reported deaths were 868 while the estimated were 3500 (World Health Organization, 2017).

Almost all the population in Sudan is at risk of malaria. The pattern of malaria transmission is seasonal and unstable. The transmission is dependent on rainfall while in urban areas, it is around the year (Federal Ministry of Health, 2017a; World Health Organization, 2017).

As in different countries the epidemiology of malaria in Sudan affected by climatic conditions such as rainfall, humidity, temperature and floods. In Sudan a wide range of climate variations is available. In North state, the temperature is the main factor affecting the epidemiology of malaria while rainfall mainly affects Savannah and South state parts. Based on the climate effect researchers found that three-quarters of the population are at risk of endemic malaria (Aal & Elshayeb, 2011; Musa, Shohaimi, Hashim, & Isthrinayagy, 2012).

In many parts of Sudan, there are irrigated agricultural projects such as AlGezeira area in central Sudan and AlGadarif in the east of Sudan. These projects

may affect the epidemiology of the disease in terms of suitable sites for mosquitoes breeding and some studies suggested a correlation between the use of agricultural pesticides and development of mosquitoes insecticides resistance (Abuelmaali et al., 2013).

Despite that malaria is a serious problem in Sudan some researchers reported underestimation of malaria burden in Sudan (Abdalla et al., 2007). Referring to the above-mentioned facts, even the epidemiology and the Plasmodium species are changing in Sudan. Increasing the efforts to achieve the goals of malaria elimination in Sudan is greatly required.

1.2.2 Malaria prevention in Sudan

Policies and strategies for malaria prevention recommend the use of insecticides treated nets (ITNs) and long-lasting insecticides treated nets (LLITNs) for all age groups and should be distributed free of charge but unfortunately, this is not in reality. Larval control and indoor residual spraying (IRS) are also of the prevention methods adopted by the WHO but insecticides resistance was started to rise as a problem that may affect the process. Resistance to some insecticides in many parts of Sudan was investigated and reported (K. A. Ahmed et al., 2015; Himeidan, Jones, & Ranson, 2011). Underuse of preventive measures in many parts of Sudan could greatly affect the process of malaria control (H. S. Mustafa et al., 2009). As appeared in the last WHO updated malaria report from Sudan intermittent preventive therapy (IPT) for prevention of malaria in pregnancy is not routinely used.

The availability, affordability and use of different prevention methods in terms of the public's behavior and stakeholder's implementation to different methods were investigated. The researchers claimed that financing and delivery of different malaria

prevention methods in Sudan should be critically reviewed as inappropriateness was noticed in many aspects (O. E. Onwujekwe et al., 2011).

1.2.3 Malaria treatment in Sudan

For many years Chloroquine remained as a cheap and effective first-line drug for malaria treatment in Sudan. Unfortunately, resistance to Chloroquine started to appear since 1978 but definite confirmation was in 1982. In 1988 a group of researchers reported in vivo and in vitro Chloroquine resistance (Abdel Hameed, 2003; Bayoumi et al., 1989). Since late 1990s many studies for confirmation of Chloroquine resistance were carried at in vivo and in vitro levels (Adam et al., 2004; Stivanello et al., 2004; van den Broek et al., 2003).

In 2004 Artemisinin-based combination therapy was introduced for malaria treatment. Artesunate -Sulphadoxine/Pyrimethamine (AS+SP) combination was selected as a first-line treatment and Artemether-Lumefantrine (AL) as a second line. The National Malaria Control Program (NMCP), WHO, General Directorate of Pharmacy (GDP) and Non-Governmental Organizations (NGOs) worked together for implementation of the new drugs guidelines as well as withdrawal of the Chloroquine from the country. The new policy was faced by many obstacles such as the cost of treatment and the availability of drugs (E. M. Malik et al., 2006).

Following implementation of the new policy, the researchers started to test the value of the new drugs in malaria treatment. The efficacy of AS+SP and AL for treatment of uncomplicated malaria in central Sudan was confirmed in a trial including 137 patients. Another study confirmed the efficacy of AS+SP in treatment of uncomplicated malaria (E. M. Malik et al., 2006; Sakina et al., 2005). The efficacy of Artesunate suppositories in treatment of severe malaria was investigated and

documented but it was not used in the routine treatment (M. I. Awad, Alkadru, Behrens, Baraka, & Eltayeb, 2003).

In malaria treatment guidelines distributed by the NMCP in 2015 uncomplicated malaria treated by AS+SP as a first line, AL as a second line and quinine as a third line. Quinine and Artemether injection were indicated for treatment of severe malaria. For Malaria treatment in pregnancy, Quinine is indicated for treatment of uncomplicated and severe malaria in the first trimester while in the second and third trimesters uncomplicated malaria treated with either Quinine or AS+SP and severe malaria treated with Quinine and Artemether (Federal Ministry of Health, 2015). In 2017 the NMCP launched new treatment guidelines for treatment of malaria in Sudan as researches reported decreased response to AS+SP (Adeel et al., 2016).

Artemether-Lumefantrine (AL) is recommended as a first-line treatment of uncomplicated malaria while Dihydroartemisinin-Piperaquine (DHAP) as a second-line treatment. For uncomplicated cases due to *P.vivax* infection AL is used and followed by Primaquine for eradication. Treatment of severe malaria is by IV Quinine or IV Artesunate. In pregnancy, Quinine is indicated for treatment of uncomplicated and severe malaria in the first trimester while in the second and third trimesters uncomplicated malaria treated with either Quinine or AL or DHAP (Federal Ministry of Health, 2017b).

1.3 Sudan Health System Profile

Sudan is 18 states which further subdivided to 184 localities. The health system in Sudan is decentralized. The Federal Ministry of Health (FMOH) with 18 states Ministries of Health (SMOH) are responsible for ensuring the Sudanese health. The FMOH responsibilities are setting national policies, overall evaluation of health

system, international relations, cadres training and controlling epidemics of national threats. SMOH responsibilities are administration and financing of the health system and hospitals management. The localities in each state manage the family health centers and units. Water and sanitation services are managed by local councils. Some of the health facilities are under the management of private sector, Ministry of Higher Education, Ministry of Interior, Ministry of Defense and National Health Insurance Fund. The total number of public health facilities is 6,183 (765 are not functioning). There are 408 general hospitals, 2020 family health centers and 3.755 health units including dispensaries. The private hospitals are 159 in addition to 18 police and 12 military hospitals. Full essential services are provided in less than one-quarter of the primary healthcare facilities. About 14% of the population has no access to the health facilities and this situation varies among different states.

The Health Information System is paper-based and the reported data vary in completeness and quality. The reporting rate varies among facilities and the data from police, military and private sector hospitals is not included in the Health Information System. Specific information systems are found in some programs such as HIV/AIDs, Tuberculosis, Malaria and Expanded Programme on Immunization, however, there is poor coordination between the programs.

Emergency and disasters management is the responsibility of the Emergency and Humanitarian Aid department which collaborate and coordinate with different governmental and non-governmental partners. Regarding malaria, this department is putting great effort in early preparedness, responding to and reducing the risk factors especially during the rainy season and conflicts emergencies (Federal Ministry of Health, 2014).

Health insurance in Sudan is provided through many providers. National Health Insurance Fund which is compulsory for formal sector employees. Khartoum State Health Insurance which covers only Khartoum state residents. The former two insurances provide services at the level of their public health facilities. Military and Police insurances provide services to the Ministry of Interior and Ministry of Defense employees and their families and they provide services at their own hospitals. Private Health Insurance Companies are also there, and they provide insurance for Private companies, International Organizations and the publics who are willing to have such type of insurance and they provide services through contracts with private hospitals. Despite the presence of different insurance providers still, a high percentage of the population is not covered by any type of insurance which makes their access to health services more difficult (A. M. A. Salim & Hamed, 2018).

The last pharmaceutical country profile in Sudan was published in 2010. It may not reflect the real current situation, but it could give an idea about the pharmaceutical services in Sudan. The licensed pharmacists were 1.53/ 10,000 population of them 0.39/10,000 population in the public sector. Pharmaceutical technicians and assistants were 0.64/10,000 population in all sectors. The licensed pharmacies were 0.59/10,000. In Sudan, there are 19 licensed pharmaceutical manufacturers. Their activities are mainly production of formulations from starting pharmaceutical materials as well as repackaging of different dosage forms. The research and development for the discovery of new active substances and starting materials in the manufacturing practices were not established yet. Drugs supplied mainly by the Central Medical Supplies Public Corporation and some private pharmaceutical importing companies. The Central Medical Supplies Public Corporation is mainly responsible for drug supply of the public sector. Registration of pharmacists, pharmacy premises,

pharmaceutical companies and pharmaceutical products in addition to the inspection of all activities related to the pharmacy profession and practices are regulated by the Medicines and Poisons Act,(2009), and the Medical Council Act (2004)(Federal Ministry of Health, 2010).

1.4 Sudan National Malaria Control Programme

Sudan Malaria Control Programme is the oldest in the tropics. Malaria control efforts started in Sudan in 1904 by Dr. A. Balfour who was tried to eradicate malaria in Khartoum through environmental control and using retained oil. After that many projects were carried such as Blue Nile Project and another program supported by Egypt to eradicate malaria in the north of Sudan. The efforts continued until launching of the Roll Back Malaria Initiative (RBM). The Sudan RBM strategic plan developed in 2002 and of its main objectives at that time was to reduce malaria morbidity and mortality to 50% by 2010 (Malik[1] & Khalafalla, 2004).

A lot of interventions and activities regarding malaria control took place in Sudan with great support from WHO, UNICEF, UNDP, Global Fund for Fighting AIDS, Tuberculosis and Malaria and many other partners. A review for the Malaria Programme was published by the Federal Ministry of Health and the Malaria Control Programme showed a perceived reduction in malaria burden between 2001 and 2012. In 2012 the reduction in case incidence was 36% compared to 2009 and 70% compared to 2000. The reported deaths decreased by 46% compared to 2009. Despite the achievements in many aspects such as case detection and management and vector control it is still difficult to conclude the exact magnitude of achievements because of incompleteness and accuracy of the data provided by the Health Management Information System (Federal Ministry of Health, 2013).

1.5 Malaria control

The process of malaria control is not an easy process and could be affected by many factors. The reports showed malaria cases and deaths were decreased worldwide however, malaria control is threatened by the emergence of resistance to ACTs started in South East Asia and insecticides resistance in Africa.(Greenwood, 2017). Despite the efforts to control malaria and availability of strategies and tools for that, it is still a major health problem especially in Africa. Estimation and tracking of malaria burden, strategies for transmission measurement, understanding of immunity and better knowledge about the mechanisms and effects of drugs and insecticides resistance where important challenges in malaria control as reported by researchers (Alonso & Tanner, 2013). Global malaria community such as governmental and non-governmental organizations, researchers, academicians, innovators, industry and funders have to accelerate the development of new insecticides and other vector control methods as mosquitoes control is a crucial step in malaria control (Hemingway et al., 2016).

Besides the vector control and effective case management, the behavior of the targeted human population is an important factor in malaria control process. In addition to that, the achievement of the disease elimination is greatly influenced by sustained political and financial commitments in the affected countries (Newby et al., 2016).

1.5.1 Effect of health services in malaria control

The responsibility of a country health system is to deliver interventions for better health outcomes for the country populations. However, in low-income countries, the limited human resources and infrastructure may constitute obstacles in delivering interventions (Atun, Lazarus, Van Damme, & Coker, 2010).

Sustainability of achievements in malaria control depends on the performance of the health systems and availability of resources. Effective malaria case management is greatly dependent on appropriate diagnosis (microscopic or rapid diagnostic tests (RDTs)) and use of treatments in accordance with the guidelines. Inefficiency of health systems in malaria services delivery was identified in many endemic countries. It was reported as limited access to healthcare facilities, inappropriate diagnosis, nonadherence of the care providers to treatment guidelines, ACTs stock outs and availability of low quality or even counterfeit and non-recommended antimalarials (Galactionova, Tediosi, De Savigny, Smith, & Tanner, 2015).

Malaria treatment should be based on appropriate diagnosis. In 2009 a study carried in central Sudan to access the diagnosis of malaria after the introduction of Artemisinin combination therapy and the study revealed that more than three-quarter of the reviewed tests were false positive which lead to overdiagnosis and overestimation of the real malaria incidence (A-Elgayoum, El-Feki, Mahgoub, El-Rayah, & Giha, 2009).

Another study carried in eastern Sudan to detect peripheral and placental malaria using microscopic and RDT and it showed inaccuracy of the RDT in that setting (Kashif et al., 2013). The above-mentioned studies revealed inappropriate malaria diagnosis. Reassurance of the quality of testing is greatly needed for better estimation of the real burden of the disease.

Appropriate treatment is an influential factor in malaria control. The availability, implementation and monitoring of valid treatment guidelines is an essential step in the cure of the disease. Implementation of the guidelines could only be possible by training of the health worker for efficient practice as well as the availability of quality assured and affordable drugs.

Five years following the introduction of ACTs to malaria treatment in Sudan, a survey was done in 15 states of the country to evaluate the practice in malaria case management. The study showed suboptimal availability of the first and second line ACTs recommended by NMCP. There was unrecommended use of monotherapy in form of Artemether injection in 25% of the surveyed cases. The study also reported poor training of health workers as well as inappropriate dispensing and counseling practices for the patients (Abdelgader et al., 2012).

Forty health centers located in Gezira state in central Sudan were surveyed after 8 years of ACTs use. Irrational use of antimalarial drugs with 9.5% use of monotherapy (Artemether injection) was also reported. The reported irrational use of antimalarials could lead to the development of drugs resistance in Sudan (Elmannan et al., 2015).

Malaria case management survey was carried out in 15 Sudanese states. About 244 public health facilities,294 health workers and 1,643 patients were included in the survey. About 88.9% of the health facilities were owned by the government. Fifty-one percent of the facilities did not have electricity while water supply was in two third of the facilities. Half of the facilities had malaria treatment charts and tables and could provide a diagnosis of malaria through microscopical examination. RDTs were found in 16% of the facilities and some facilities could perform both methods of malaria testing. Less than half of the patients were tested for malaria. Use of non-recommended monotherapy (Artemether injection), presumptive treatment in 17% of the patients and inadequate dispensing and counseling practices were also reported. Antimalarials recommended by NMCP were stocked in majority of the surveyed facilities; however; suboptimal availability of first and second line treatments was reported. Expired drugs were stocked in seven facilities. Chloroquine was stocked in 5% of the facilities despite that it was withdrawn from malaria treatment regimens five years before the survey.

The main providers of health care were medical assistants of whom 52.7% received training by NMCP on ACTs use and only 23.5% on RDTs use. The study showed suboptimal malaria diagnosis and treatment practices (Abdelgader et al., 2012).

Another study for assessment of malaria case management in children under five years was conducted in one of the teaching hospitals in Khartoum. The study showed that less than fifty percent of febrile children (43.7%) were tested for malaria and only 22% of them had a positive malaria test. The microscopical examination was the main method of malaria testing, however, RDTs were done for some patients. Five of the children who had a positive malaria test did not receive antimalarial. Eight of children with negative tests and ten of those who were not tested for malaria were treated presumptively for malaria. Two third of the children treated for malaria, intravenous Quinine was given despite that signs of severe malaria were not present at admission. The rest of patients treated by either AS+SP or AL. Generally, the study revealed poor adherence to malaria treatment guidelines (Bilal et al., 2015).

The above studies showed that the pattern of health system related constraints in malaria control in Sudan was not different from those reported in many endemic African countries.

Despite that implementation and monitoring of malaria treatment guidelines should be audited by the NMCP, there is no a lot of published studies in Sudan that investigated the real practices of malaria treatment and antimalarial drugs used in hospitals as well as identification of the antimalarials drugs related problems that could affect the treatment outcomes.

Sudan is a very big country in which the accessibility to health services could vary in different places. For example, the pastoral tribes usually move with their animals from place to another during dry and rainy seasons which make their reach to

health facilities very difficult and sometimes could be impossible. In many parts of Sudan community pharmacies are accessible to a great portion of the community. As in many African countries, publics do seek malaria treatment in community pharmacies, this could raise many questions such as are they provided with the appropriate treatment? Do the community pharmacists have the knowledge and training that qualified them for providing malaria treatment? Does malaria treatment by community pharmacists affect the process of malaria control negatively or positively?

A recently published research in Sudan showed that the community pharmacists do dispense antimalarials without prescriptions. However, the researchers did not investigate the community pharmacists knowledge and training regarding malaria prevention and treatment practices (Elgizoli & Salim, 2017).

1.5.2 Effect of community behavior in malaria control

Despite that community participation played significant roles in some diseases control in many countries, its role in malaria control is not fully realized (Atkinson, Vallely, Fitzgerald, Whittaker, & Tanner, 2011).

The community contribution in the process of malaria control is an important component that could not be ignored. Their use of prevention methods and treatment seeking behavior are important factors in malaria control. Delivering interventions for malaria prevention and control in a community-based manner were proofed to be an effective method for reducing malaria burden. (Salam, Das, Lassi, & Bhutta, 2014).

The practice of malaria self-medications among Sudanese community was reported by few researchers (A. Awad, Eltayeb, Matowe, & Thalib, 2005) (A.I. Awad & Eltayeb, 2007). Underuse of Insecticides treated nets was also reported in some parts

of Sudan (Hassan, Malik, Okoued, & Eltayeb, 2008) (O. B. Osman, Hamad, M.,, Ahmmed, & Ahmed, 2015). However, the publics knowledge about the disease and antimalarial drug use behavior regarding compliance to treatment, their handling of drugs related problems and their knowledge and use of malaria prevention methods were not largely investigated.

Now Sudan is one of the countries that controlling malaria (Newby et al., 2016). Malaria control is an integrated process that requires the contribution of the stakeholders, health workers and the community. If not, all come together roll back malaria will not come to reality. It took short time to change the treatment guidelines in Sudan from Artesunate+ Sulphadoxine / Pyrimethamine as a first line treatment in 2015 to Artemether-Lumefantrine in 2017 compared to Chloroquine which remained for decades as the first-line drug for malaria treatment (Federal Ministry of Health, 2015, 2017b). That could be due to irrational use of drugs or many other factors, therefore, identification of the obstacles in the way of malaria control is the first step for malaria elimination in Sudan.

1.6 Barriers to malaria control

Despite the efforts to control malaria, still the disease mortality and morbidities were higher especially in sub-Saharan African countries. The researchers tried to identify the barriers of malaria prevention and treatment. They related some barriers to communities' knowledge. Poor knowledge about the disease causes and symptoms was still reported in many countries. Prevention related barriers were reported in terms of affordability and use of preventive methods in addition to the peoples believe that malaria is non preventable disease. Treatment related barriers were accessibility to health facilities and the quality of care provided. Compliance to treatment and

treatment cost were other obstacles of malaria control. Treatment related wrong believes such as that convulsions due to severe disease is spiritual and should be treated by traditional healers. Some communities have concern about the effectiveness of treatment at hospitals and efficacy and use of medications (Maslove et al., 2009).

Another group of researchers tried to identify the barriers at the level of policy making. They reviewed the literatures and interviewed policy makers and stakeholders in three East African countries (Kenya, Uganda and Tanzania). They mentioned some barriers that were related to individual's characteristics and behaviors such as disease knowledge, adherence to malaria control regimens and cultural believes. Poverty and limited resources could not be ignored. Health system related barriers were mainly related to accessibility to health care facilities, availability of drugs and other malaria control measures. Health systems capacities, organization, infrastructures and research priorities were also of the identified barriers. Financial resources constitute a major determinant of the decision-making process in malaria control. The cost of malaria control materials and drugs regimens determination and implementation is high as it requires training at all levels from approval to diagnosis and prescribing. The policy process of malaria control is fragmented process that require collaboration of different ministries such as Health, Environment and many other partners (Paul et al., 2015).

Different patterns of malaria transmissions may exist at one country or one region. That could be an obstacle in the way of malaria control. It was suggested that malaria control programs should design different malaria control policies that suits the ecological, environmental and social needs of each area. Additional prevention methods such as malaria seasonal chemoprevention, genetic modification of mosquitoes, mosquito traps as well as transmission blocking drugs and vaccines should be implemented (Greenwood, 2017).

1.7 Rationale of the Study

By the broad cause of death malaria, HIV and tuberculosis are the top killing disease in Sudan as reported by WHO. The process of malaria control is a complex process and could be achievable only by appropriate prevention and treatment which need collaboration between community and healthcare professionals. In Sudan community pharmacists are contributing in the process of malaria prevention and treatment as the situation in many Asian and African countries but there was no a lot of published research in Sudan that elaborated this role. Elgizoli & Salim, (2017) published a research showed that community pharmacists in Khartoum were dispensing antimalarials without prescriptions, however; they did not evaluate the knowledge of pharmacists regarding malaria and its prevention and treatment. This will be the first study to assess the knowledge, and practice of the community pharmacists in malaria prevention, treatment and reporting of antimalarial drugs ADRs. Now in Sudan, we are in a transitional stage to the concept of pharmacist patient-oriented practice and still many people are looking for the pharmacist as drug dispenser rather than care provider. The community perception to the role of the pharmacist in malaria treatment will be investigated. The community knowledge about malaria prevention and antimalarials use behavior is an important component of malaria control because unless the community awareness about the disease and its prevention and treatment is good enough the control will not be accomplished. This may raise many questions regarding malaria control such as:

1-Is malaria appropriately treated in public hospitals?

2-Do the community pharmacists have the knowledge about malaria prevention and treatment?

3-Do the community pharmacists practice regarding antimalarials dispensing affecting the malaria control process negatively or positively?

4-Do the public have the knowledge about malaria prevention and treatment?

5-Is the antimalarials use behavior among the public affect the malaria control process negatively or positively?

The findings of the study could show the situation of malaria prevention and treatment in Khartoum and could help in suggesting solutions for malaria control.

1.8 Study Objectives

1.8.1 General objective

Identification of barriers to effective prevention and treatment of malaria in Khartoum, Sudan.

1.8.2 Specific objectives

1- Assessment of the effect and contribution of pharmaceutical services in malaria prevention and treatment by assessing of the community pharmacist knowledge and practice in prevention and treatment of malaria.

2- Assessment of the perception of the community pharmacists to their role in malaria prevention and treatment and their role in reporting ADRs of antimalarials.

3- Assessment of the public's knowledge, and practice regarding malaria prevention and treatment.

4- Assessment of the public's perception to the role of community pharmacist in malaria prevention and treatment

5- Evaluation of malaria treatment in a public hospital setting with special consideration to ADRs and drugs interactions reporting and management.

CHAPTER 2

LITERATURE REVIEW

2.1 Malaria economic burden

2.1.1 Global burden

Funding for malaria control and elimination is increasing annually with up to one-third of this fund provided by endemic countries governments. Contribution of international fund in malaria elimination and control could be provided as a direct aid to endemic countries or through Global Fund, World Bank or other institution. Part of the fund directed to malaria research in many fields such as antimalarial medicines which took the majority of research funding as well the research in malaria vaccines and basic research (World Health Organization, 2017).

The relation between malaria and poverty was studied in different countries. Researchers related malaria and poverty in many aspects. Increased incidence of malaria was reported among poor people lives in houses built from deciduous materials and of poor hygiene. Residing far from health services and inability to pay for the prevention and treatment services were also of the factors led to increased incidence, morbidity and mortality of the disease among poor communities (Bi & Tong, 2014; Obaldia, 2015; Sonko et al., 2014; Yadav, Dhiman, Rabha, Saikia, & Veer, 2014).

African countries suffer high economic burden of malaria. Studies were carried in many countries to estimate this problem. Hospital and households' surveys were carried in Nigeria to estimate the cost of treatment and the economic burden of the disease. Majority of the surveyed populations were farmers. The results showed that the cost of treatment was a real problem not only for the poor community but also to the health system (Ibitoye, Shaibu, Sanda, & Ajayi, 2016; O. Onwujekwe et al., 2013).

In Malawi, the cost of malaria treatment was assessed for inpatients. The high cost of treatment exceeds the average daily income of majority of the Malawians. The days lost from work for the patients and their caregivers and the days lost from school were also considered as a part of the economic burden of the disease. The high cost of treatment may affect the treatment-seeking behavior of the patients and the control of malaria in such poor communities (Hennessee et al., 2017).

The economic burden of malaria in six African countries (Chad, Mali, Nigeria, Rwanda, Ghana, and Uganda) was assessed between 2002 and 2005. The researchers reported that malaria had a significant negative effect on the economic growth of the studied countries. They recommended that increasing investment in malaria control could help in the development of poor communities in African countries (Okorosobo, Okorosobo, Mwabu, Orem, & Kirigia, 2011).

Private sectors investment in malaria control in collaboration with international agencies and local governments of endemic countries will improve the economic development of these countries as it will increase the efficiency of employees as well as directing the spending to development and education.(Purdy, Robinson, Wei, & Rublin, 2013).The relationship between increasing income and malaria reduction in 100 countries was studied and a positive relation was reported (Datta & Reimer, 2013).

2.1.2 Malaria burden in Sudan

Sudan is classified as middle to low-income country; therefore, the cost of malaria treatment could be a real burden and it will have an obvious impact in economic. The cost of treatment is usually assessed as a direct cost which includes medical consultation, investigations, hospitalization and drugs. Indirect cost could be

expressed in terms of morbidities, mortalities and days lost from work or school for both patients and caregivers (M. H. Mustafa & Babiker, 2007).

Gezira state is one of the most important agricultural areas in Sudan because most of the crops with high economic return (such as cotton) are grown there. The effect of malaria on farmers' productivity was investigated. The researchers reported a loss of farmers' efficiency and working hours which greatly affected their economic status because agriculture was their main source of income. The reduction in farmers productivity could have a negative impact on the country economy (Nur, 1993).

Malaria care expenditure was estimated in Wad-Medani central Sudan (it is the capital of Gezira state). The cost of treatment was calculated for hospitalized patients (adults and children) and outpatients. It was found that the cost of treatment in hospitalized patients was more than the patients who treated at home. Treatment in private settings was more costly than public settings. The bulk of the cost of treatment was the cost of medications. The researchers concluded that the cost of malaria treatment was a burden for all socioeconomic classes (Abdel-Hameed, Abdalla, & Alnaury, 2001).

The cost of malaria treatment in public health centers and private pharmacies was assessed in six Sudanese states (Khartoum, River Nile, Red Sea, Northern Kordofan, Southern Darfur and Gadarif). The research revealed that the patients spent an average cost of about 2 days of their lowest government salary for their malaria treatment. There was a slight increase in the cost of treatment in private pharmacies compared to public health centers (Cheraghali & Idries, 2009).

In 2004 a household survey was carried in Khartoum state to estimate the economic burden of malaria. The direct and indirect cost of treatment was found to be a real burden especially in households who were not working in government or even

private formal sectors because they were not covered by health insurance and majority of them were paid on daily basis. The research revealed that the medication cost was the higher followed by consultation fees. Treatment cost was higher in private clinics compared to public health centers and hospitals (M. H. Mustafa & Babiker, 2007).

The economic burden of malaria in three areas of Khartoum was also studied. Families of different socioeconomic status were assessed for their income, environment in their homes and surroundings, their treatment seeking behavior and use of preventive measures. High prevalence of the disease and inappropriate treatment seeking was reported in families with low income (Mahgoub, 2017).

A study carried in Sinnar state, Sudan showed that the cost of treatment was a real obstacle in malaria control. Researchers suggested that reduction of the treatment fees could be of great value in improving the treatment-seeking behavior of the community (Abdu, Mohammed, Bashier, & Eriksson, 2004).

2.2 Community perception of malaria and its treatment

Control of diseases in different communities could be affected by the social and cultural behaviors and practices of the community. Researches showed a lot of differences in the communities' knowledge, attitudes and practices in malaria prevention and treatment.

In Ghana, a survey was carried in two villages. The people there have their own names to malaria, they called it "Pua". They failed to describe the adequate relation between malaria, mosquitos and stagnant water. Part of the surveyed people could mention some malaria symptoms. The respondents mentioned that bed nets could be used for prevention of nuisance rather than malaria. They believe that anemia and convulsions were spiritual diseases that mainly treated by traditional healers. Some