The Etiology of Malaria Scourge: A Comparative Study of Endemic Nations of Africa and Asia

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Abstract: The aim of this study is to conduct a comparative study of malaria infections in endemic areas of Asia and Africa and to profer new strategies that will be useful in curtailing the disease. Malaria varies greatly around the world in the level of intensity, in the mosquito vectors that transmit it and in the species causing the disease. P. vivax appears to be more widespread among 20 countries in Asia while the fatal P. falciparum are widely spread in about 50 countries in Africa. A keen observation around most hospitals in Nigeria and Africa in general show that many patients are plagued by malaria as it accounts to the highest percentage of in-patient and out-patient treatment cases, compared to other diseases. Africa including parts of Asia suffers infrastructural decay and poverty occasioned by malaria burden which seems to have defied many solutions for complete eradication. The method employed specific comparative studies along the line of geographical distribution and etiology to determine the spread, use socio-economic mobility assessment and behavioural risk factors to distinguish situation in both Asia and Africa. Also we considered commitments in local control efforts around the continents of Asia and Africa. While noting that P. vivax is more prevalent in Asia than in Africa where P. falciparum is common we conclude that an assessment of global initiative impacts are notable in more in Africa and the trend of mobility of Asians for economic reasons tend to increase their susceptibility rate to the infection. Due to comparative differences between African and Asian regions as addressed in this work, the translation of global malaria control strategy into regional and country-specific strategies will help bring a modified implementation of unique and beneficial control techniques for the disease eradication.

Key words: Developing nations, malaria, mosquito nets, P. falciparum, epidemiology

INTRODUCTION

Fatal human malaria infection is initiated when an infected Anopheles mosquito Anopheles gambiae, injects sporozoites during a human blood meal. After injection, sporozoites enter the bloodstream and go to the liver, where they invade hepatocytes and develop into exoerythrocytic forms (Coppi et al., 2005). These liver stage parasites are asymptomatic but when matured, they are released into the Red Blood Cell (RBC) for erythrocytic stage, a form characterized with symptomatic malaria.

Drug resistance in evolving Plasmodium falciparum strains and insecticide resistance of the female Anopheles mosquito account for major biomedical catastrophe standing against all effort to eradicate malaria in Sub-Saharan Africa. Malaria is endemic to more than 100 countries and by far the most costly in terms of human health causing major losses among many Asian and African nations including Thailand, Indonesia, Nigeria, Tanzania etc. Plasmodium species is a protozoan parasite that infects approximately 500 million people annually, killing more than one million, mainly children and pregnant women in Africa (Le Roch et al., 2003; Breeman, 2001). Malaria is a global problem as estimates suggest that 40% of the world’s population is at risk of malaria (Brown and Reeder, 2002).

There are three main strategies presently attempting to control malaria disease: vaccination, vector control and drugs. Of these, drug application is currently the main line of disease control with some level of mosquito control. Despite initially promising results with multicomponent recombinant protein vaccines targeted against the asexual blood stages (Gordon et al., 1995) and vaccines directed against the sporozoite stage (Bojang et al., 2001), effective immunization against the disease is not yet available (Yeh et al., 2004). There is however, a deepening crisis with emerging resistance among malaria parasites to the existing drugs. For these reasons, it is imperative that new lines of drugs be explored before existing drugs lose too much efficacy (Ralph et al., 2001) and comparative studies in geographical distribution, disease etiology, socio-economic and behavioural risk factors as studied in this paper will serve as current trends for development and improvement of control strategies in the continents of both Asia and Africa.
ETIOLOGICAL AND GEOGRAPHICAL ISSUES OF HUMAN MALARIA

The kind of species of *Plasmodium* in a particular area will determine the kind of treatment and the avalanche of available control measures to choose as an applicable approach in an area. Plaguing parts of the continent of Asia and Africa is the Apicomplexa protozoan parasite, *Plasmodium* sp. identified as the causative agent of the malaria disease. The Apicomplexa are a large group of protists, most of which possess a unique organelle called apicoplast and an apical complex structure involved in penetrating a host's haemocyte and red blood cell. There are four species of malaria parasites which infect people namely *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. Severe *falciparum* malaria has a case-fatality rate of around 10% in reasonably well-equipped hospitals (http://pinoymalaria.wordpress.com/location/). Malaria caused by *P. vivax* is acute but not life-threatening illness associated with anemia and splenomegaly and causes low birth weight. Moreover, the liver stages of *P. vivax* can give rise to relapse.

*P. vivax* has the widest geographical range as it is present in sub-tropics, several temperate zones and also coexists with *P. falciparum* several parts of Africa and in tropical parts of the Americas and Asia. The most fatal malaria parasite, *P. falciparum* is the commonest species throughout the tropics and sub-tropics and predominates in sub-Saharan Africa. Some species like *P. malariae* has a similar geographical distribution with *P. falciparum* but is far less common and its incidence is patchy. However, *P. ovale* occurs in Africa and sporadically in south-east Asia and western Pacific (http://pinoymalaria.wordpress.com/location/). However, there is very low incidence of malaria in North African countries and they are sometimes designated as malaria free. Besides, according to WHO, half of all malaria cases in Thailand are in its four southernmost provinces-Songkhla, Pattani, Yala and Narathiwat. The other half are among migrant workers and displaced people from Myanmar, Laos and Cambodia along the border. Despite different levels of spread and transmission, Table 1 clearly depict regional categorization of member countries in Africa where the malaria disease is endemic. For easy assessment and comparative studies, a similar table for different regional categories was also studied for malaria situation in Asia and this is shown in Table 2 (http://www.rollbackmalaria.org/gmap/3-2.html). These have helped to show the spread in terms of regional categories of malaria endemic countries in both Africa and Asia. Out of the listed countries, 35 countries are in high transmission areas in Africa while 11 out of the listed Asian countries are in high transmission areas. Low-burden countries includes: Botswana, Cape Verde, Namibia, South Africa, Swaziland and Zimbabwe.

In the rest of Asia, none of the 35 countries that account for 98% of estimated malaria deaths worldwide are located in the Middle East and Eurasia. However, within the region, the burden is highly concentrated: almost 100% of deaths and 97% of cases are concentrated in three countries-Pakistan, Yemen and Afghanistan (http://www.rollbackmalaria.org/gmap).

**COMPARATIVE MALARIA ACTIVITIES IN AFRICA AND ASIA**

Due to differences in regions malaria activities may sometimes vary in endemic areas in the two continents. A critical analysis of these activities will help to identify needed and effective approach peculiar to each region in terms of curative measures and vector control.

**Targets:** The target for 2010 in sub-Saharan Africa is to reduce malaria mortality and morbidity by 50%, meaning Africa will reduce its burden to approximately 158 million cases and 480 thousand deaths, based on the 2000 incidence and mortality numbers. By 2015, the objective
is to reduce the morbidity to 79 million cases and reach near zero mortality for all preventable deaths (http://www.rollbackmalaria.org/gmap/3-2.html). Beyond 2015, the objective is to maintain near zero mortality for all preventable deaths. While this target is challenging, it is possible and will go a long way to achieving the global targets since Africa bears 71% of global malaria cases. An analysis of 20 high-burden African countries (http://www.rollbackmalaria.org/gmap/3-2.html) shows that if 2010 coverage goals are met and sustained, over 4.2 million total lives will be saved by 2015. This equates to over 600,000 lives saved per year in these 20 countries alone.

In India, Indonesia, Myanmar, Viet Nam and Bangladesh, ~91% of the population at risk lives in areas of high transmission of both P. vivax and P. falciparum while the remaining ~23% live in moderate to high transmission. P. vivax is endemic in all 20 countries. P. falciparum is found in all countries except DPR Korea and Republic of Korea. Indonesia has the highest burden area in the easternmost provinces. Thailand has a large proportion of its burden concentrated in border areas (http://www.rollbackmalaria.org/gmap/3-1.html).

**Drugs and malarial treatment:** In 2009, 19 new molecular entities (NMEs) and 6 biologic license applications (BLAs) were approved by the FDA’s Center for Drug Evaluation and Research (CDER)-1 more than in 2008. Just one out of these is Artemether-lumefantrine (Coartem) from Novartis for malaria treatment (Hughes, 2010). These recent drug products are distributed for use in endemic areas of Asia and Africa. However, many plant species across Nigeria, Madagascar, Kenya, Mali and other African countries continue to be used in traditional medicines for the treatment of malaria and many people depend on such remedies as they cannot afford effective antimalarial drug needed to treat chloroquine-resistant *Plasmodium falciparum* infections. The natural products of these plant origins ranging from alkaloids, terpenes, quinines, methanol and miscellaneous compounds can provide lead compounds for conventional drug development.

In a number of African countries, studies have shown that the emergence of chloroquine resistant malaria parasites is associated with two-fold increase in malaria deaths. However, a study in Momp, Senegal revealed that malaria mortality in children under 4 years increased 11-fold within 6 years of chloroquine resistance (Trape et al., 2002). In Nigeria, the leaves or bark of *Erythrina senegalensis, Pterocissus eleta, Cassia alata, Bridelia micrantha, Lophira alata, Adonisia digita and Nauclea latifolia* are used for malarial treatment (Ajayieoba et al., 2004) while in Madagascar, *Strychnos myrtoides* plant is used as an adjuvant with chloroquine (Rasosanaivo et al., 1994). The extracts of *Pittosporum viridiflorum, Fuerstia Africana, Schkuhria pinnata, Clerodendrum eriophyllum and Ludwigia erecta* were reported to be in use by members of Meru district communities of Kenya (Muthaura et al., 2007). A climbing shrub called *C. sanguinolenta* has a number of indoloquinoline alkaloids including cryptolepine as a major constituent with antiplasmodial property (Cimanga et al., 1997). A decoction of its roots is used to treat malaria in West Africa (Boyde and Ampeño, 1983) despite a reported DNA synthesis inhibition (Bonjean et al., 1999). Toxicity, poor oral bioavailability of cryptolepine (Wright, 2005; Wright et al., 1996; Klayman, 1985).

Chinese scientists in 1972 isolated artemisinin, an usual endoperoxide sesquiterpenelactone as an active principle from *Artemisia annua* (Asteraceae) and it was quickly shown to be a rapidly acting antimalarial drug effective against chloroquine resistant parasites (Wright, 2005; Klayman, 1985). Clinical studies of traditional antimalaria ethanolic extract of *A. annua* formulated into tablets and capsules were used to treat 144 malaria patients in China in 1992 resulting to reduced parasitaemia after 3 days (Yao-De et al., 1992; Wright, 2005). Furthermore, the administration of *A. annua* herbal tea on 48 Democratic Republic of Congo malaria patients revealing 92% reduced symptoms after 4 days (Mueller et al., 2000).

In 2009, World Health Organization with support from a variety of donors and partners, has taken a leading role in efforts to characterize and contain artemisinin resistance in South-East Asia. Three of the things urgently need to do: (1) halt the manufacture, marketing and use of oral artemisinin monotherapies, (2) provide universal access to diagnostic testing for malaria and (3) strengthen routine surveillance for malaria and regular monitoring of antimalarial drug efficacy. Drug resistance or re-infection of patients may not be the only problem but cases of reemergence where malaria seem to re-emerge after initial treatment due to failure of the drug to kill completely all the parasites after first treatment (Osamor et al., 2009b; Fehintola et al., 2007). In this case, those parasites that survive continue to multiply so that after a few weeks the patient again experiences malaria symptoms. The situation may perhaps be associated with the relative short half lives of commonly used artemisinin derivatives and the non-responsiveness of malaria parasite early blood stages (Osamor et al., 2010a, 2009b) to these resistant drugs cases (Wright, 2005; Wright and Warhurst, 2002). Some countries are using innovative
malaria treatments: since 2002 DPR Korea has employed mass prophylaxis of primaquine against P. vivax in targeted populations.

**Insecticide Treated Nets (ITN) and Long Lasting Insecticidal Nets (LLINs):** ITNs and LLINs are both bed nets used to prevent and repel mosquitoes against direct contact with human skin to discourage biting and causing infection. However, while ITNs require more frequent treatment because its treatment is ephemeral, LLIN is long lasting for several years (http://www.netmarkafrica.org/Countries/). In 2008 manufacturers reported the delivery of 1.5 million LLINs to Nigeria, but the national programme reported distributing nearly 7 million (WHO, 2009). Some of the difference might be accounted for by delivery of nets to private sector enterprises. The number of nets needed to cover all persons at risk in high-burden countries in 2008 was approximately 336 million (one half of the 671 million persons at risk, assuming that one net covers two persons). The cumulative number of LLINs delivered in 2006-2008 by manufacturers was 1.41 million, which represents 42% of the 336 million needed in 2008 (assuming a lifespan of 3 years). Data from ministries of health indicate that an estimated 35% of the nets needed were distributed (WHO, 2009). AED Netmark, a US company engaged in private-public partnership for sustainable malaria prevention is responsible for liaising with various governments agency especially in provision of affordable and free mosquito net in Sub-Saharan Africa. NetMark has a representation in Nigeria, Ghana, Senegal, Mali, Ethiopia, Uganda, Zambia (http://www.netmarkafrica.org/Countries/).

In a study on the acceptability of LLINs in two communities in India, Gunasekaran et al. (2009) reported that seasonal variation in influences the use of bed net. During summer, many people did not use bed nets as they used to sleep in open space to avoid heat inside their houses. During winter, people used blankets to protect them from cold and mosquito bites. This and the habit of sleeping near fire for warmth lend the bed nets unused. Only during rainy season, with their restricted activity outdoors and abundant mosquitoes, people used bed nets regularly. Other benefits perceived were undisturbed sleep at night (17.3%), reduced fever/malaria (15.5%) and finding only fewer mosquitoes inside houses at night (3.6%).

**Disbursement of fund for malaria control:** Malaria fund disbursements by external agencies per person at risk for malaria in relation to the size of the population at risk, show that huge investment goes to Africa, followed by America and lastly Asia. Some countries receive more external assistance than others with equivalent populations at risk (e.g., Gambia, Kenya and Malawi). Other countries, such as Cape Verde, Congo and Brazil, are outliers from the overall trend and appear to have lower levels of external funding even after their size is taken into account.

It suggests that smaller countries (such as Sao Tome and Principe, Suriname and Vanuatu) receive more funds per capita than larger countries (such as China, India and Pakistan). The pattern of funding whereby smaller countries receive higher per capita amounts may be appropriate if malaria programmes for smaller populations have proportionally higher fixed costs; however, programmes in smaller countries may also have lower costs for distribution of commodities such as ITNs, ACTs and diagnostics. An obstacle to increasing funding in larger countries is affordability (WHO, 2009).

**Market removal of oral artemisinin-based monotherapy:** More collaboration and involvement of national drug regulatory authorities is required to implement the resolution and to ensure complete elimination of oral artemisinin-based monotherapy medicines from all countries as stipulated by resolution WHA 60.18. The private-sector pharmaceutical markets in many malaria-endemic countries are unregulated, pharmaceutical companies tend to ignore the WHO guidelines of removal of artemisinin-based monotherapies. Moreover, when responsible companies comply with the recommendation by withdrawing their oral artemisinin-based monotherapies from the market, they leave “niche markets”, which are exploited by faceless opportunistic companies manufacturing substandard products to perpetrate their acts.

While 24 malaria-endemic countries have either never registered or have taken regulatory measures to withdraw marketing authorizations for these medicines and another 11 countries have declared their intention to comply with the WHO recommendation, 41 countries still allowed marketing of these products as of the end of 2008 (WHO, 2009). However, this implementation is challenging in many African countries and parts of Asia due to weak or absence of regulatory body. Indian pharmaceutical manufacturers’ produces about 70% of malaria drugs shipped into African countries. As part of the implementation of resolution WHA 60.18, WHO 2009 intimated the India government through her Director General for Drug Administration on need to phase-out the production of oral artemisinin-based monotherapy due to resistance problem. This resulted in compliance forced by pronouncement of penalty and withdrawal of licenses of erring companies.
House proofing with windows screens, ceilings and blocking of eaves: *Anopheles gambiae* mosquitoes transmit *P. falciparum* and are well adapted for entering houses because they fly upwards when encountering a vertical surface (Snow, 1987). *Anopheles gambiae* is attracted by human odor from inside the house and they typically reach the wall, travel vertically along its surface and then enter through the eave gap between the wall and the roof. This observation is reinforced by studies showing that houses with open eaves and those lacking ceilings are associated with increased mosquito numbers and higher levels of malaria compared to the ones with closed eaves and the ones with ceilings (Ogoma et al., 2009a; Kirby et al., 2008; Lindsay et al., 2002).

Blocking of specific entry points for mosquitoes into houses is regularly practiced by human subjects consciously and unconsciously in homes today. A cross-sectional household surveys conducted in urban Dar es Salaam, Tanzania by Ogoma et al. (2009c) estimated the usage levels of available options for house proofing against mosquito entry, namely window screens, ceilings and blocking of eaves. This situation is directly linked to poverty and the availability of houses for citizenry.

Development in Asia is relatively higher than in Africa and fewer people that live in Africa can barely afford conducive homes that are less prone to mosquito bite which transmits malaria. Nigeria and most African countries live below poverty line with large number of people homeless. This affords incessant mosquito bite on individuals that live outside or in open spaces.

**SOCIO-ECONOMIC AND BEHAVIOURAL RISK ACTIVITIES OF MALARIA**

**Social and economic impact:** Malaria debilitation has marginalized the poor and made them quite vulnerable as it affects socio-economic development adversely. According to the World Health Report 2001, malaria leads to an estimated loss of 1.87 million Disability Adjusted Life Years (DALYs) in South East Asian Regions countries each year. This amounts to a direct or indirect loss of about 3 billion US Dollars (USD) every year (WHO, 2005).

The statistics of Bathurst (2008) elucidated the social and economic impact of malaria and it is highlighted below:

- Annual lost GDP for Africa: $1.5 billion
- Costs up to 40% of total public health expenditure
- Is the cause of up to 50% of in-patient and outpatient care
- Costs up to 60% of total household expenditure

This alarming statistics on the threat of malaria have spun global interest to set up initiatives with spelt out responsibilities and goals to combat the malaria pandemic as stated in the work of Osamor (2009a, b).

**Social and behavioral impact:** It was demonstrated that these risk factors can be broadly divided into three groups: (1) social and behavioral risk factors (Osamor, 2010b) favoring increased occurrence and transmission, i.e., poor housing conditions, population movements, irregular or non-use of mosquito nets, partial or non-conformance with residual DDT spraying, etc. (2) behavioral risk factors predisposing to severe and complicated malaria (not clearly known, probably delayed treatment) and (3) behavioral risk factors related to occurrence of drug resistance, i.e., treatment-seeking patterns, practices of drug utilization and population movements. In Kenya and most African countries, most people sleep under a net throughout the year, while a few only used a net when mosquitoes are abundant. Bush clearing was the second most common method that community members practiced (Opiyo et al., 2007). We are in agreement with Opiyo et al. (2007), that the major reasons believed to be responsible for malaria infection by local communities in most developing countries include unfavourable weather conditions (cold temperatures, change of weather from cold to hot or vice versa, when one is rained on, sitting in the sun for too long, at times of new moon). It also include lack of hygiene (drinking of dirty water, walking barefoot in dirty environment, unhygienic conditions at home, badly ventilated house, dirty utensils, dust, lack of a latrine or rubbish pit), a bushy compound (planting crops next to the house, bushes and high grass on the compound), food (raw, cold, contaminated or processed food) and body exhaustion (hard labour, no sleep, starving, fever).

**THE LOCAL COLLABORATIVE NETWORK EFFORT IN MALARIA MANAGEMENT**

Malaria comes in wide variations hence requires a stratified, area-specific strategies for effective and sustainable control. There are several ecological subtypes of malaria in many countries and continents. These include malaria in forests and forest fringes, irrigation malaria, development project malaria, malaria in migrant
population and urban malaria (WHO, 2005). These varied infection methods are also at the receiving end by the formation of various collaborative networks on malaria (Osamor, 2010a).

The Asian Collaborative Network for Malaria (ACTMalaria) is a major malaria fighting network in Asia. Currently, ACTmalaria is collaborating with and the Bureau of Vector Borne Disease (BVBD), Department of Disease Control, Ministry of Public Health, Bangkok, Thailand to launch the seventh international training on the Management of Malaria Field Operations (MMFO) holding on 20 September to 19 November 2010 in Bangkok, Thailand. Their curriculum is performance-based training, using current educational approach such as problem-based and inquiry-led learning that allows participants to develop critical thinking and life-long learning skills. Such Network is expected to be self-sustaining to be able to fight malaria efficiently.

In Nigeria (Jeremiah et al., 2008) the option of malaria treatment at PHC is delayed till the advent of complication and near death. This was attributed to difficulty with access to health centre, scarcity of affordable drugs including antimalarial drugs, perceived deficiencies in the performance of formal health services including poor clinical skills, attitude of health personnel and cultural beliefs (WHO/UNICEF, 2003, Feyisetan et al., 1997). This practice increases morbidity and mortality in addition to contributing to possible emergence of drug resistance (WHO/UNICEF, 2003; Ajayi et al., 2008).

In Africa there are varied collaborative networks on malaria management. We have E8 regional Network as a result of increase collaboration among the eight neighboring countries, to achieve their common goal of eventual elimination of malaria in the region and elimination in four countries, Botswana, Namibia, South Africa and Swaziland, by 2015. The E8 includes these four countries, along with their other four northern neighbors, Angola, Mozambique, Zambia and Zimbabwe. The idea behind the enlarged Elimination Eight (E8) is that four southernmost malaria countries in southern Africa can only successfully eliminate malaria, if the countries immediately to their north also focus their efforts on scaled-up malaria control along their southern borders.

In 1995, African Malaria Vaccine Testing Network (AMVTN) started its activities but later metamorphosed into The African Malaria Network Trust (AMANET) in 2002. Their initial primary goal is the preparation of Africa in the plan and conduct of malaria vaccine trials. They have now expanded beyond that singular goal in malaria interventions to incorporate an integrated approach like research and development and general malaria intervention in Africa. AMANET is based in Tanzania and currently houses the Multilateral Initiative on Malaria (MIM).

CONCLUSIONS

By this study, a comparative situation study has been carried out to elucidate malaria infection from both Asian and African perspectives. Having given account of the etiology, it is quite obvious that disease vary slightly with P. falciparum devastation in Africa than in Asia. We also pinpointed the fact that more of the global initiative funding of malaria projects goes more to Africa than Asia due to reasons of severity level and the population at risk. However, the socio-economic and behavioural disposition seems similar in both continents where the disease is endemic, we conclude that Asians have more of migrant population that move from place to place due to job and economic opportunities that influence infection level. Poverty is more in Africa and the geographical location harbours the survival of the vector more than in Asia and technology to fight malaria is growing faster in Asia. Above all, collaborative networks targeted at malaria eradication are flaming more in Africa than in Asia partly due to the commitment of growing global initiatives involvement in control strategies. In a coordinated effort, research base in Africa is comparatively improving technologically both in internet and software development (Osamor et al., 2010b) and also along the line of sensor networks (Daramola et al., 2008). While trailing Asian technology, Africa is also improving in high-throughput technological research (Osamor, 2009a) equipped with novel clustering techniques (Osamor et al., 2009a, b) for addressing the biology of malaria parasite to uncover approaches that will help in its eradication. Only time will tell before we can see the end of malaria.

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