A SURVEY OF THE STATUS OF MALARIA IN GUYANA AND TREATMENTS: SYNTHETIC AND HERBAL

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ABSTRACT

Malaria is an infectious disease characterized by recurring attacks of chills and fever, induced by the bite of an anopheles mosquito, infected with any of four protozoans of the genus *Plasmodium: P. vivax, P. falciparum, P. malariae, or P. ovale*). In Guyana and Worldwide, Malaria is a leading cause of infection deaths induced by vectors. It affects both the young and old, and if not taken seriously, it can prove fatal. According to the World Malaria Report 2011, by the World Health Organization (WHO), ‘there were 216 million cases of malaria and an estimated 655 000 deaths in 2010. Malaria mortality rates have fallen by more than 25% globally, since 2000 and by 33% in the WHO African Region. In Guyana, within the eleven year period from 2000 to 2010, the numbers of new cases of Malaria reported has shown variation with a general decrease. From the period 2000 to 2005, a general increase is noted with a maximum value of 38,984 in 2005 from an initial value of 24,018 in 2000. A general decrease was noted from 2005 to 2010 with the number of persons infected in 2010 being 22,935. The lowest number of 11,657 was observed in 2007. These values are significant and thus appropriate Health Standard Protocols should be followed in Guyana to curb Malaria. Both synthetic and herbal treatments are used to treat Malaria in Guyana and Globally.

Keywords: Malaria, infectious disease, World Health Organisation, Plasmodium species, Ministry of Health.

1. INTRODUCTION

Malaria is an infectious disease characterized by recurring attacks of chills and fever. It is induced by the bite of an anopheles mosquito which is infected with any of four protozoans of the genus Plasmodium with a characteristic life cycle1,2. The four protozoans are *P. vivax, P. falciparum, P. malariae, or P. ovale* 1. Malaria causes disease through a number of pathways depending on the species. *Plasmodium vivax* and *Plasmodium falciparum* are the most common, with *Plasmodium falciparum*, being the most deadly to the diagnostic cycles of fever which characterize malaria. *Plasmodium vivax*, for example, tends to produce cycles of fever every two days, whereas *Plasmodium malariae* produces fever every three. Malaria, can also be transmitted by a contaminated needle, blood transfusion, organ transplants and needle sticks3,7,8,24. With regards to the mode of action (MOA), *Plasmodium falciparum* infects red blood cells (RBC) and changes their structure. Infected RBC then binds to the walls of blood vessels and tissues (brain and lungs) via sequestration, allowing the malaria parasite to replicate. Infected RBC can also bind to non-infected RBCs, forming clumps of rosettes that results in the narrowing of blood vessels, leading to fatality. The formation of rosettes is mediated by the PfEMP1 protein5.

The malaria parasite is transmitted exclusively by the female anopheles mosquito3,7,8,24. The intensity of transmission depends on the condition of the environment, the human host, the vector and their breeding conditions. Anopheles mosquito’s breed in water while each species may have their own preferences. Some may prefer shallow collections of fresh water, such as puddles, rice fields, and hoof prints. Transmission can be more intense, based on the life cycle of the mosquito, i.e. if the lifespan is longer so as to allow the complete development of the parasite in its vector and where it prefers to bite humans rather than animals. It is also dependent on the climatic conditions such as rainfall patterns, temperature and humidity, as it may affect the number and survival of the mosquitoes. In many places, transmission is seasonal, with the peak during and just after the rainy season. Malaria epidemics can occur when climate and other conditions suddenly favour transmission in areas where people have little or no immunity to malaria. They can also occur when people with low immunity move into areas with intense malaria transmission, for instance to find work, or as refugees. In Guyana, malaria is prevalent in the interiors since many residents often go there, seeking job opportunities. Many natives residing there are also affected as they are out of reach due to lack of electricity and telephone lines as a way of educating their population.

Symptoms of malaria include: Fever, Headache, Chills, Vomiting, Muscle aches, Diarrhea, Coughing, Sweating, Enlarged spleen. Infection by *Plasmodium falciparum*, if not treated immediately can lead to severe illness and often
results in death. Sign and symptoms of infection by this species include: Bleeding problems, Shock, Liver or kidney failure, Central nervous System problems, Coma, Cerebral malaria (coma, or altered mental status or seizures, anemia. There are three types of malarial fever based on symptoms and the organism causing the attack. These include: Tertian Fever, Quartan Fever, Malignant Fever. Malaria is referred to as an ‘acute febrile illness.’ In a normal, unsuspecting, non immune individual, symptoms appear seven days or more (usually 10–15 days) after the infective mosquito bite.

Researchers and scientists around the world have not yet established an effective vaccine to control the spread of malaria but. However, several are under development. Glaxo Smith Kline, a renowned pharmaceutical manufacturer, has proven to half the risk of African children from getting malaria during the clinical trial of what is likely to become the world’s first vaccine against the disease. Scientists stressed that the vaccine known as RTS,S or Mosquirix, is no quick fix for eradicating the disease and is no less effective against it than other vaccines are against common infections such as polio and measles.

Recently, it has been shown that Heparin modified atomic force microscope (AFM) tip binds specifically to infected red blood cells through interaction with the PfEMP1 protein, but not to uninfected cells. Haparin is a very strong candidate for malaria treatment because it has anti-malaria activity by itself. It also has specific targeting abilities and a strong interaction with plasmodium infected red blood cell. Heparin could be used to carry more potent antimalarials to their target sites.

In Guyana, malaria affects both old and young and if appropriate measures are not taken, the disease can be fatal. This paper describes the status of malaria in Guyana and its treatment via synthetic and herbal means.

Procedure: (a) Sample collection: Statistical data for malaria between the period 2000 to 2010 were collected from the Ministry of Health and were analysed.

Results: The following results were obtained from the Georgetown Public hospital from the period of 2000 to 2010.

<table>
<thead>
<tr>
<th>Year</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>Average, X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of New Cases</td>
<td>24018</td>
<td>27122</td>
<td>21872</td>
<td>27627</td>
<td>28866</td>
<td>38984</td>
<td>21064</td>
<td>11657</td>
<td>11815</td>
<td>13673</td>
<td>22935</td>
<td>22693.90909 ± 4851.977241</td>
</tr>
</tbody>
</table>

The Standard Deviation (SD), Variance and Confidence Limit (CL) was found to be ± 8210.30, 67409026.09 and CL (µ)= 22693.90909 ± 4851.977241 and respectively.
Fig. 1.0. Bar chart showing the number of persons infected with malaria per year in Guyana between the year 2000 to 2010 (Courtesy of the Georgetown Public Hospital, GPH, 2012)
Map of Guyana showing Status of Malaria induced by *Plasmodium Falciparum* in 2010
2. DISCUSSION
The data above shows the number of persons infected with malaria over the period 2000 to 2010. The year 2000 register 24,018 malaria cases and this increased to 27122 in 2001. A decline was noted in 2002. From 2003 to 2005, there was a significant increase with the highest value of $38,984 been registered in 2005. This high increase in 2005 was probably due to one of the largest floods in Guyana’s history. Many water borne diseases were rampant. It was an opportunity for mosquitoes of all species to multiply. Malaria was one of the vector diseases that were noticeably on the increase. There was a decline in 2006 to 2008, with the lowest value of 11, 815 been recorded in 2008. This general decrease was probably due to the drastic measures undertaken by the government of Guyana to combat malaria.

After the flood, the next year there was a significant decrease in the number of new cases reported. This was due to proper control of the vector. The government of Guyana through its Ministry of Health has resorted to promoting education of their citizens about malaria. They distributed insecticide impregnated nets especially in the interiors where malaria is prominent, which may have lead to a decrease. Again, from the period 2009 to 2010. Values was 13, 673 and 22, 935 respectively. The average number of persons infected with malaria within the eleven year period is calculated to be 22,693.90909 with a standard deviation of 22693.90909 ± 8210.30 and variance of 67409026.09. The confidence interval (CI) was calculated to be 22693.90909 ± 4851.977241.

The welcoming decrease from 2006 was probably due to control methods being put into effect and actually being utilized by those in areas that are prone. This was a good initiative to reduce the new cases reported per year. However, in 2009 and 2010, the numbers increased once again, proving to the government that they need to educate the population more on malaria and its effects and make treatment more readily available.

Malaria is one of the leading cause of deaths worldwide. It occurs in tropical and subtropical countries where the distribution is determined by the presence of the anopheles mosquito and appropriate temperature which allows the parasite to complete its life cycle.

In Guyana, there is high risk throughout the year especially in the interior areas, near to Brazil, with sporadic cases in the densely populated coastal belt. The following population groups are at risk for malaria:

- Young children in stable transmission areas who have not yet developed protective immunity against the most severe forms of the disease;
- Non-immune pregnant women as malaria causes high rates of miscarriage (up to 60% in P. falciparum infection) and maternal death rates of 10–50%);
- Semi-immune pregnant women in areas of high transmission. Malaria can result in miscarriage and low birth weight, especially during first and second pregnancies. An estimated 200 000 infants die annually as a result of malaria infection during pregnancy;
- Semi-immune HIV-infected pregnant women in stable transmission areas, during all pregnancies. Women with malaria infection of the placenta also have a higher risk of passing HIV infection to their newborns;
- People with HIV/AIDS;
- International travelers from non-endemic areas because they lack immunity;
- Immigrants from endemic areas and their children living in non-endemic areas and returning to their home countries to visit friends and relatives are similarly at risk because of waning or absent immunity.

Malaria can be prevented by sound policies, drugs and herbal treatments. The WHO lists the following policies that are used to prevent malaria:

- Integrated Vector Management (IVM)
- Indoor Residual Spraying (IRS)
- Insecticide Treated Materials

Proper environmental sanitation may also reduce the risk of contracting this disease. This includes cleaning drains and alley ways regularly; releasing stagnant water and pouring oil in waterways that are stagnant and cannot be cleared often. Integrated Vector Management (IVM) seeks to improve the cost-effectiveness, efficacy, ecological soundness and sustainability of disease-vector control. The characteristics of this method include:

- Selection of proven vector control methods based on knowledge of local vector Biology and Ecology, disease transmission and morbidity;
- Utilization of a range of interventions, separately or in combination and often synergistically;
- Collaboration within the health sector and with other public and private sectors that impact on vector breeding;
- Engagement with local communities and other stakeholders;
- A public health regulatory and legislative framework;
- Rational use of insecticides;
• Good management practices.

The IVM approach considers the available health infrastructure, resources and combines all available and effective measures, whether chemical, biological, or environmental. It also encourages an integrated approach to disease control. Indoor residual spraying (IRS) seeks to reduce transmission by reducing the survival of malaria vectors entering houses or sleeping units. It includes the use of insecticides that vectors are susceptible to. According to the WHO, the IRS method remains valuable when the following conditions are met:

• High percentage of the structures in an operational area have adequate sprayable surfaces, and can be expected to be well sprayed;
• Majority of the vector population is endophilic, i.e. rests indoors;
• Vector is susceptible to the insecticide in use.

Insecticide treated materials include simple actions such as sleeping under mosquito impregnated nets. Sprays containing permethrin are safe to use on clothing, while sprays containing DEET can be used on skin. To date, 37,000 long lasting insecticide treated nets have been distributed in the malaria endemic regions of Guyana. Fogging can be done in residential areas once residents are alerted. One common way of preventing mosquitoes in Guyana, is by “smoking them out”. This can be done by lighting a fire of grass and leaves in an area where it can be controlled and pose no risk to the community. It is said the smoke drives the mosquitoes away. Window screens can also be used to prevent mosquitoes from entering buildings. Wearing long pants and long sleeve tops during the peak of mosquito activity (between dusk and dawn) and light colored clothing may also help.

Amongst the synthetic drugs used to combat malaria are: Chloroquine, Proguanil, Maloprim, Mefloquine (Lariam), Doxycycline and Malarone. Only Chloroquine will be discussed here. Chloroquine, has been the drug of choice for both treatment and Chemoprophylaxis of malaria since the 1940’s and has remained the drug of choice for P. falciparum and other species of human malaria parasites, except in regions where P. falciparum is resistant. It is most used anti-malarial drug and is dispensed as Chloroquine Diphosphate, a water soluble powder with a bitter taste. It binds to Ferriprotoporphyrin IX, a breakdown product of hemoglobin digestion by the malaria parasite. Free Ferriprotoporphyrin IX is toxic to cells, causing lysis of the erythrocyte and intracellular parasites. The parasite is able to complex this heme product to endogenous binding sites to prevent lysis.

Chloroquine is effective in terminating acute clinical attacks of malaria. It is a suppressive agent against all malarias except those strains of P. falciparum that are Chloroquine resistant. It lowers fever within 24-48 hours and by 48-72 hours after treatment parasites are no longer found in the blood. It can also be used to treat amebic liver abscess when it reaches high liver concentrations.

With regards to herbal treatment, Artemisinin/Qinghaosu or Sweet Wormwood, is the active drug in the Chinese medicinal herb Artemisia annua. It was isolated in 1971. The WHO gave high priority to development of fast acting artemisinin derivatives for the treatment of cerebral malaria and for the control of multi-drug resistant falciparum malaria. A water soluble ester called artesunate and two oil soluble preparations called arteether (artemotil) have now been developed. Artemisinin derivatives act by inhibiting a P. falciparum, encoded sarcoplasmic-endoplasmic reticulum calcium ATPase. Most of the clinically important artemisinins are metabolised to dihydroartemisinin (elimination half-life of about 45 min), where they have comparable antimalarial activity. The short half-lives of artemisinins limit the possibility of resistance. A Pharmaceutical company, Sanofi, uses genetically engineered yeast that convert glucose into artemisin acid. The latter is converted into Artemisinin via four steps as show in scheme 1.0.
Herbs Used in Guyana to combat malaria include St. John Bush, Justicia secunda, Aloe Vera, Aloe barbadensis, Fit-Weed- Eryngium foetidum, Aspidosperma excelsum, Bitter Tally, Mikania hookeriana, Tamarind, Tamarindia indicus, Papaw/ Papaya- Carica papaya. Herbal doctors and Amerindians (indigenous people) use these herbs in various concoctions to treat the symptoms of malaria. Some may use the whole plant or pieces such as the leaves, the stem, or the bark. The plants used are known to have antiparasitic properties which make them effective against the malaria parasite[15].

3. CONCLUSIONS AND RECOMMENDATIONS
From the research, it can be concluded that malaria has not been successfully eradicated from Guyana. It may have been eradicated along the coastal areas but not in the hinterland areas. Guyana has a long history of malaria cases and the Government is interested in reducing this record. The highest numbers of cases are from the hinterland due to many mining camps being established and attracting workers from all regions of Guyana. The highest record of malaria cases was reported in 2005 as Guyana suffered at the hands of many diseases that were on the increase and rampant during the flood brought on by heavy rainfalls. The Government of Guyana, through its Ministry of Health should try to educate the population by reaching out through various mediums such as the internet, television or by hosting workshops in the susceptible areas and promote awareness of the disease and ways to protect them and their families and prevent the vector from entering their homes and surroundings. They should also fog more often and distribute insecticide impregnated materials in such areas also.

The citizens should take it upon themselves to keep their environment clean and healthy by cleaning drains regularly, releasing stagnant water sources and clearing bushy areas to get rid of the vector. They should also wear protective clothing, use mosquito nets and repellants.

In areas where there is resistance to certain drugs such as chloroquine, a combination technique of elimination and control of such vectors should be devised. Monitoring and surveillance should be increased to evaluate the threat of resistance. Also, access to diagnostic and treatment should be more accessible in Guyana. The Government should construct infrastructure and offer such services in areas where malaria is prevalent; especially in the hinterland areas.

4. ACKNOWLEDGEMENTS
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5. REFERENCES

Artemisinic acid
Artemisinin

Scheme 1.0, The conversion of Artemisinic acid to Artemisinin


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