

Malaria 16th leading cause of death worldwide

Alka Awasthi¹, Iqbaljit Kaur^{1*}, Srijana Sharma¹, Keerti Bhardwaj¹, Tarun Madaan¹

Department of Pharmaceutics, School of Pharmaceutical Sciences, Lovely Professional University, Phagwara,
Punjab, India, 144411

Abstract

Malaria is an attack that usually starts with shivering and chills, followed by a high fever. Protozoan is the main cause for such infectious disease. The most targeted ones are the third-world countries, with millions of diseases and infections which leads to millions of deaths. There have been attempts to control the disease in which pesticides and drugs are used. The treatment of malaria and its prevention have been launched with new techniques and are under development, including vaccines. The nets that are treated with insecticide have found to be beneficial. the placental malaria and low birth weight declination has been observed. However, this causes drift of fetal , maternal, and infant morbidity and mortality . The resistance to plasmodium falciparum is naturally acquired by the women over successive pregnancies, as the antibodies are naturally formed by the women against the parasite and the parasitized red cells bind to chondroitin sulfate A in the placenta which indicate that a vaccine is feasible [1]. In such alarming situation, effective diagnostic methods are essential for the control and management of malaria. This review details the currently available literature for malaria [2].

Keywords: Plasmodium; techniques; pregnancy; diagnosis and placenta.

Introduction

The parasitic protozoan Plasmodium is responsible for malaria. It spreads through indirect contact of person to each other by the means of bite of a septic Anopheles mosquito. It multiplied in the liver and pass infection to erythrocytes in the body. Individuals residing in underprivileged nations are highly susceptible to this disease. The general symptoms of this disease consist of high body temperature, nausea & headache.

If proper treatment is not given then, it can be life threatening. By using bed nets impregnated with insecticide and IRS (Indoor residual spraying) with insecticide, malaria can be prevented malaria to some extent. Normally, Antimalarial agents such as artemisinin-based combination therapies (ACTs) are given to treat malaria. But now the parasites have become resistant to some antimalarial agents in most of the parts around the globe [3].

Causes of Malaria

Protozoa of the genus *Plasmodium* is responsible to cause malaria. There are four Plasmodium species which are responsible to cause disease in humans such as *P. malariae*, *P vivax*, *P ovale* and *P falciparum*. Plasmodium's other species infect birds, reptiles as well as mammals. It spreads to individuals by the bite of *Anopheles* female mosquitoes [4].

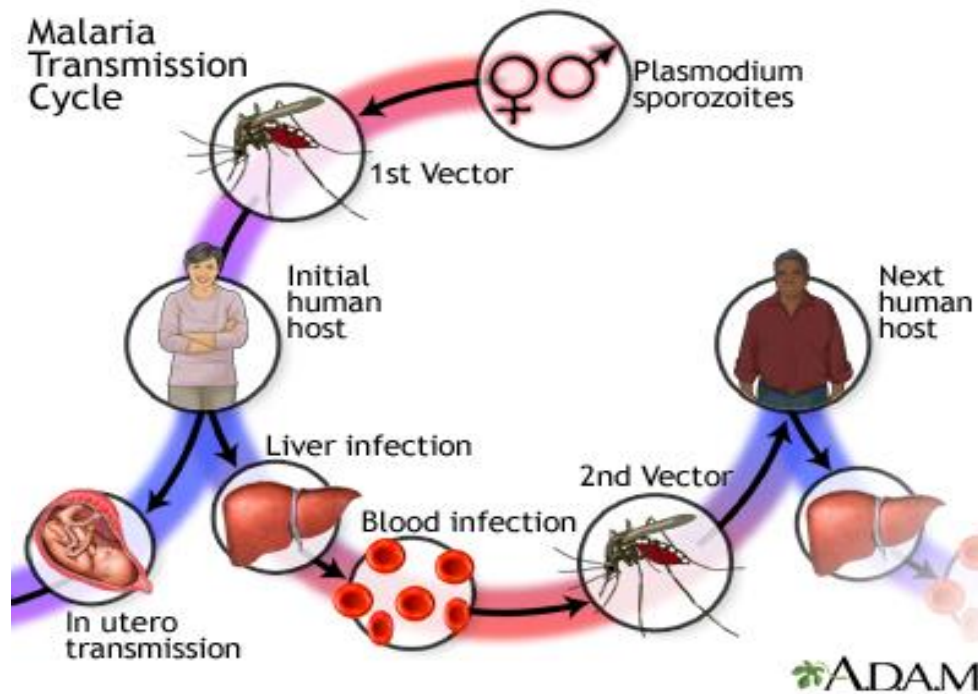


Fig. 1 depicts cause of Malaria

Life cycle

Life cycle of malaria is an example of cyclic transmission disease between human and female *Anopheles* mosquitoes. It grows in the liver of human and then moves to erythrocytes. Afterwards, erythrocytes are being destroyed by the continuous brooding parasites results in the formation of daughter parasites called merozoites which further penetrates into the remaining blood erythrocytes and cycles continuous.

Blood stage parasites are responsible for the clinical manifestation of malaria. When female *Anopheles* mosquito ingested specific kinds of blood stage parasites (gametocytes, which take place in male and female kinds), they start to grow and replicate by mating in the intestine of the mosquito. After 10-18 days, a kind of parasite named as sporozoite makes their way to the salivary glands of the mosquito. At the time *Anopheles* mosquito draws a blood meal on other individual, anticoagulant saliva is injected combined with sporozoites, which transmit to the liver & results in the birth of novel cycle.

Therefore, the septic mosquito act as a carrier of the disease between two individuals known as "vector". The individuals who got infected they transfer the parasite to the mosquito; the mosquito vector is unaffected by the parasite as compare to human host for which it is very harmful [5].

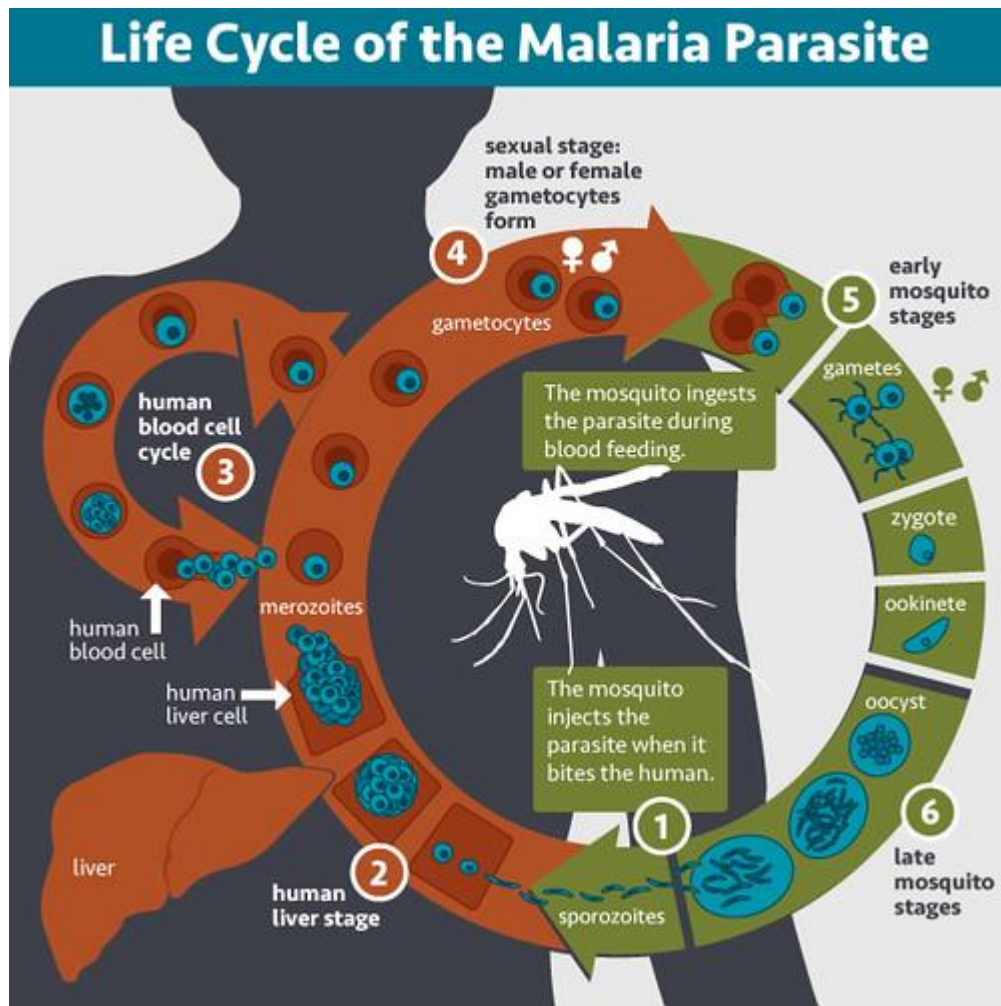


Fig. 2 depicts life cycle of Malarial parasite [13]

Pathogenesis

The rupturing of erythrocytes cause chills and fever in host body. If there is plasmodium falciparum which is responsible for severe malaria it blocks capillaries and post capillary venules and cause sickness, suffocation and release some toxic products. In case of cerebral malaria, there is blockage of circulation in the brain and other organs and it leads to complications in the host body [6].

Host Defences

Both acquired and innate immunity occur. Innate immunity is composed of various erythrocytes traits which reduce the risk of infection. The sickle-cell trait prevents the development of severe *P falciparum* malaria, and the absence of Duffy antigen prevents infection cause by *P vivax*. Recurrent infections lead to the development of humoral and cellular immune responses against all *Plasmodium* stages [7].

Symptoms of Malaria

- Chills
- High temperature
- Vomiting
- Sweating

- Fatigue
- Dry Cough
- Pain
- Nausea
- Headache
- Enlargement of spleen
- Acute kidney injury
- Hyperparasitemia
- Low blood pressure
- Metabolic acidosis
- Acute respiratory distress syndrome (ARDS)
- Hypoglycaemia
- Severe anaemia
- Haemoglobinuria [7]

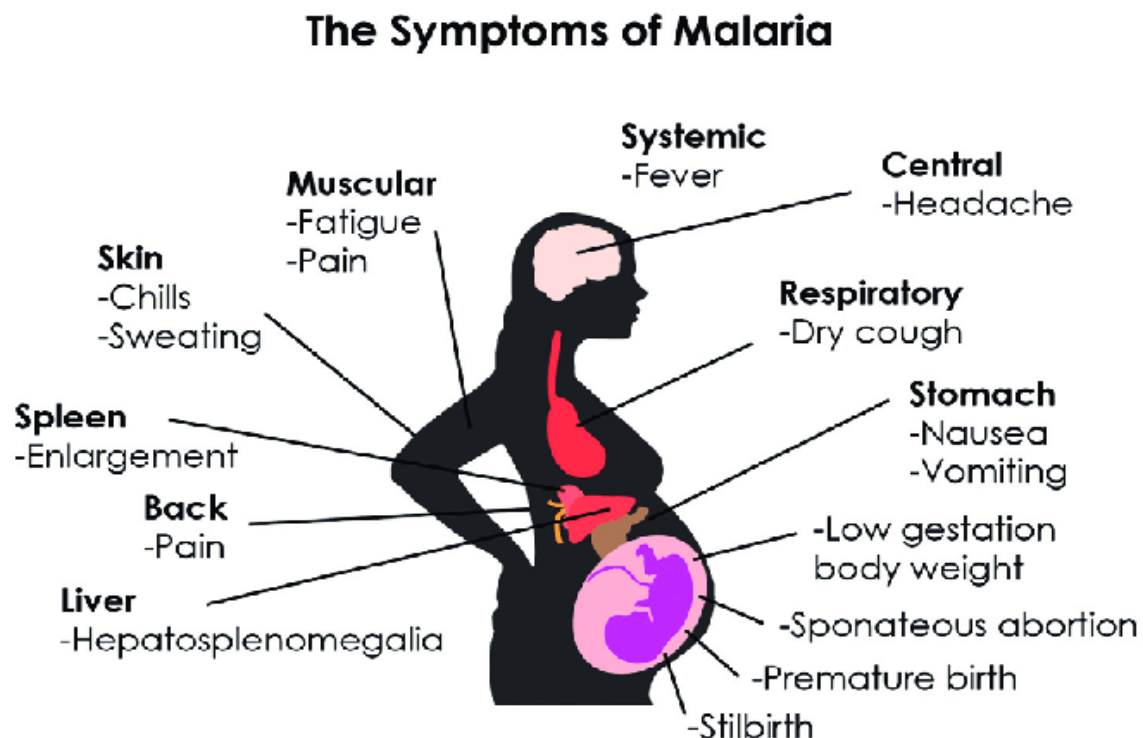


Fig. 5 depicts symptoms of Malaria in pregnancy

1. *P. falciparum* is responsible for low birth weight infant or premature delivery
2. *P. vivax* malaria can cause spleen rupture rarely [1]

Diagnosis

The consequences of delayed analysis as well as therapy leads to increase mortality rate due to malaria in the globe. If any person has high body temperature, visit to an endemic area for malaria or receive infected blood through IV route should be considered as malaria. Moreover, person history must be analysed for malaria because malaria infected population shows 1^o illness after the exposure within 6 weeks, sometimes it extends to a year or 2-3 years [2].

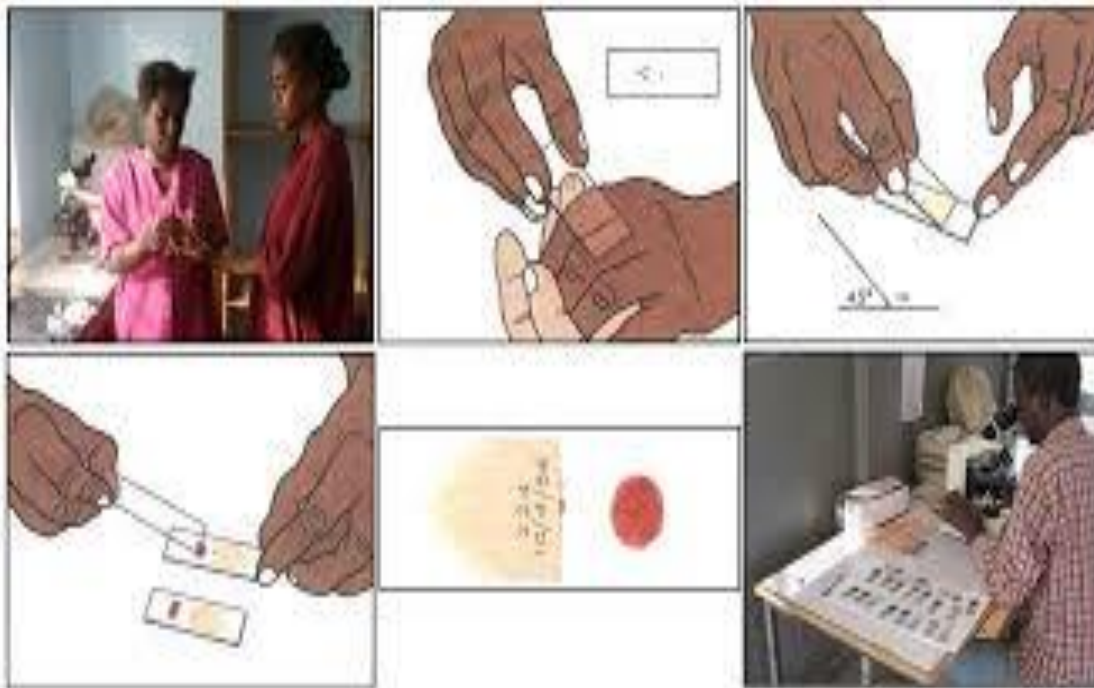


Fig. 4 depicts diagnosis of Malaria

If malaria is diagnosed then the blood samples of infected person should be analysed every 6 to 12 hours for at least 2 days. Novel diagnostic techniques are developed that consist of detecting parasites with a fluorescent stain and a rapid antigen-capture dipstick test. These latest techniques offer various merits like rapid, easy to perform, highly specific and sensitive. Other detective methods involve PCR (Polymerase Chain Reaction), malaria antigens and antibodies and DNA/RNA probe techniques [6].

Malarial Control [8]

S.No.	Methods to prevent malaria	Description
1.	Anti-malarial drugs	Antimalarial drugs are utilised to treat malaria like pyrimethamine, doxycycline, primaquine, and proguanil by inhibiting the entry of parasites into systemic circulation. Others drug include mefloquine, quinine, sulfadoxinepyrimethamine, and chloroquine kill the parasite within erythrocytes.

2.	Source Reduction	Elimination of larva development site is possible by manipulating and modification of specific area's environment where malaria incidence chances could be more due to human actions like public works, irrigation etc.
3.	Laryciding	In order to kill mosquitoes in the larval stage are biological and chemical methods. Petroleum oils (Paris green) and pesticides such as temephos and fenthion are considered as chemical larvicides. Biological methods employ larvivorous fish
4.	Spraying	Any methods that may shorten the life span of mosquitoes should also probability of malaria transmission. Residual insecticides can be utilised to kill indoor mosquitoes but for outdoor ones, localized outdoor spray is effective. It is unfortunate that mosquitoes became resistant to these pesticides in many parts of the globe.
5.	Contact Reduction	Several ways are opted to reduce the contact of human and mosquito with the help of mosquito coils, protective clothing, bed nets and insect repellents.

Effective States of Malaria (India)

Historically, in India *Plasmodium vivax* predominantly caused malaria, which lead to 53% of the cases. In 1990s, there was a spread of drug-resistant *Plasmodium falciparum*.

The proportion of *P. vivax* had decreased to 34% nationally in 2014, it caused around 380,000 malaria cases in India. *Plasmodium vivax* has developed resistant against the control methods in urban areas. *P. vivax* is the main subject to outbreaks which predominantly causes urban malaria, which is linked to enhanced death rate and is activated by bursts of migration and construction. Moreover, the parasites potential and transmission maintenance are re-established by the hypnozoite reservoir in areas which was thought to be eradicated due to variable malaria eco-epidemiological profiles and few transmission factors, the malaria causes a lot of burden to India. This review describes epidemiological trends of *P.vivax* malaria in India with attention to four states : Gujarat , Karnataka , Haryana and Odisha [9].

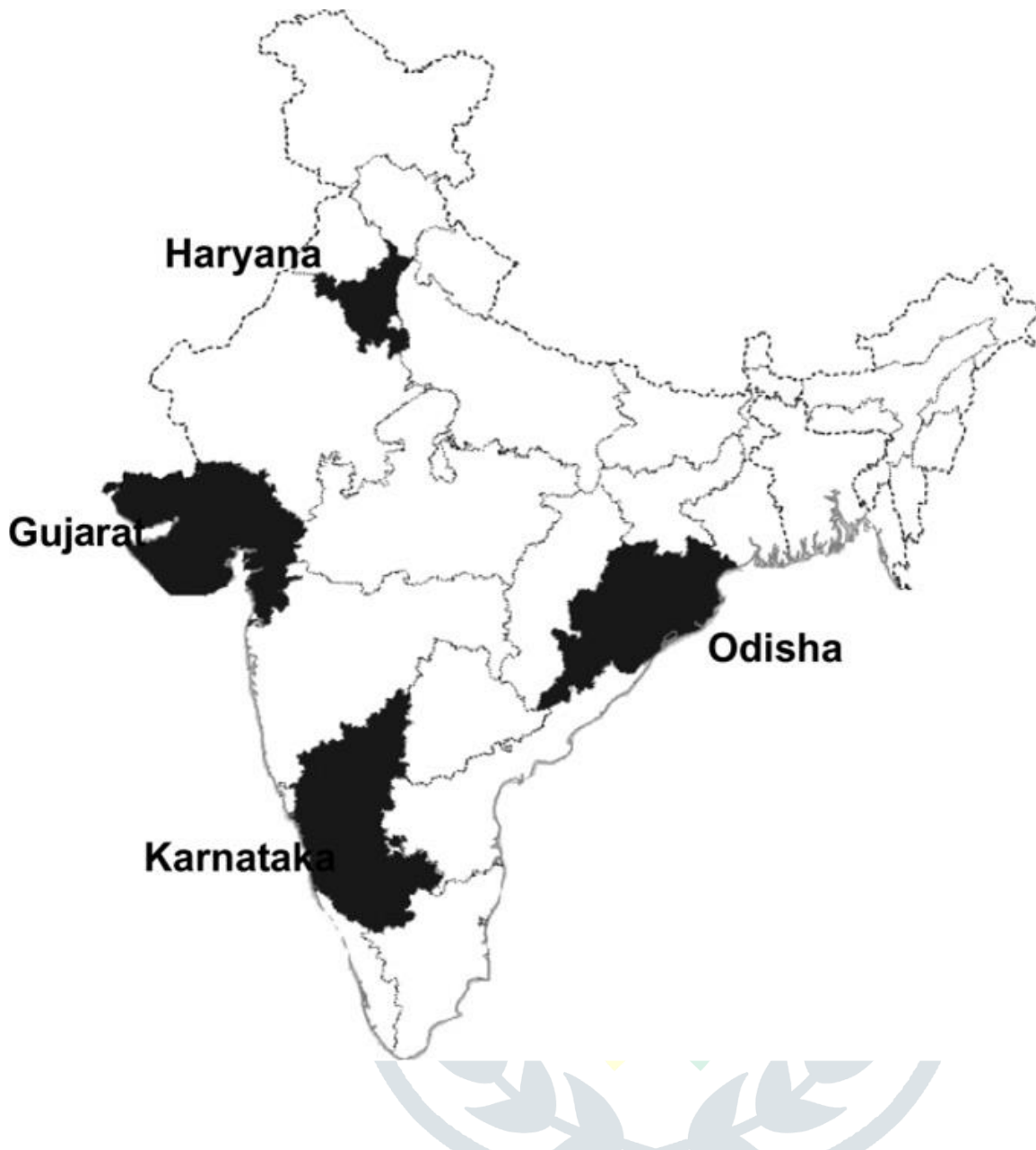


Fig. 9 depicts Map showing most effective states of India

Table 1 Some herbal plants use in treatment of Malaria worldwide [10,11]

S.No.	Common name	Parts Used	Scientific Name (Species)	Family
1	Ginger	Rhizome	<i>Zingiber officinale</i>	<i>Zingiberaceae</i>

2	Neem	Bark, leaves	<i>Azadirachta indica</i>	<i>Meliaceae</i>
3	Lime	Root, leaves, fruit, stem-twigs, bark	<i>Citrus aurantifolia</i>	<i>Rutaceae</i>
4	Mahogany	Bark	<i>Khaya grandifoliola</i>	<i>Meliaceae</i>
5	Mango	Bark, leaves	<i>Mangifera indica</i>	<i>Anacardiaceae</i>
6	Guava	Bark, leaf	<i>Psidium guajava</i>	<i>Myrtaceae</i>
7	Senna	Bark	<i>Senna siamea</i>	<i>Caesalpinaceae</i>
8	Siam weed	Root, leaves	<i>Chromolaena odorata</i>	<i>Caricaceae</i>
9	African yellow wood	Bark	<i>Enantia chlorantia</i>	<i>Annonaceae</i>
10	Iroko	Root, bark	<i>Melicia excels</i>	<i>Moraceae</i>
11	Pawpaw	Leaves, fruit	<i>carica papaya</i>	<i>Caricaceae</i>
12	African peach	Root, bark, leaves	<i>Nauclea latifolia</i>	<i>Rubiaceae</i>
13	Tree marigold	Leaves, stem, twigs	<i>Tithonia diversifolia</i>	<i>Compositae</i>
14	Turmeric	Rhizome	<i>Curcuma longa</i>	<i>Zingiberaceae</i>

Conclusion

Malaria has become the most common health concerned issue as the data reported that this parasitic disease cause infection to approximately 225 million population and also cause 1 million mortality per year. These digits are enhancing due to resistance developed by infected mosquitoes against antibiotics and insecticides. Additionally,

if the disease is not regulated with the suitable control methods then it indirectly allows the transmission of disease to others. Therefore, it can conclude that Malaria is leading cause of death worldwide [12].

Reference

1. Fried M and Duffy P.E. Malaria during pregnancy. *Cold Spring Harb Perspect Med.* 2017 Jun; 7(6): a025551.
2. Tangpukdee N, Duangdee C, Wilairatana P, Krudsood S. Malaria diagnosis: a brief review. *The Korean journal of parasitology.* 2009 Jun;47(2):93.
3. <https://www.who.int/tdr/diseases-topics/malaria/en/>
4. <https://www.cdc.gov/malaria/about/biology/index.html>
5. <https://www.ncbi.nlm.nih.gov/books/NBK8584>
6. <https://www.cdc.gov/malaria/about/disease.html>
7. <https://www.ncbi.nlm.nih.gov/books/>
8. Sharma RK, Thakor HG, Saha KB, Sonal GS, Dhariwal AC, Singh N. Malaria situation in India with special reference to tribal areas. *The Indian journal of medical research.* 2015 May;141(5):537.
9. [https://www.who.int/malaria/publications/world-malaria-report-2018/report/en/Effective years of Malaria/](https://www.who.int/malaria/publications/world-malaria-report-2018/report/en/Effective%20years%20of%20Malaria/) accessed on 19 November 2018 at 5 pm.
10. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2816451/Medicinal plants useful for Malaria/By Ibukun E. Aibinu, Peter O. Fabeku/African Journal of Traditional, complementary and Alternative Medicines/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2816451/Medicinal%20plants%20useful%20for%20Malaria/By%20Ibukun%20E.%20Aibinu,%20Peter%20O.%20Fabeku/African%20Journal%20of%20Traditional,%20complementary%20and%20Alternative%20Medicines/) accessed on 13 November 2006/ vol.4/ page no.191-198.
11. [http://dx.doi.org/10.4314/ejhs.v28i5.17/Mango,Ginger/By Sultan Suleiman, Bart De Spigella/ Antimalarial activities of mango, ginger/Journal of Pharmacognosy and Phytochemistry/](http://dx.doi.org/10.4314/ejhs.v28i5.17/Mango,Ginger/By%20Sultan%20Suleiman,%20Bart%20De%20Spigella/Antimalarial%20activities%20of%20mango,%20ginger/Journal%20of%20Pharmacognosy%20and%20Phytochemistry/) vol. 28/ issue no. 5 / accessed on 1 September 2016.
12. <https://www.ncbi.nlm.nih.gov/books/NBK215638/>