A REVIEW: ON THE STATUS AND TREATMENT OF MALARIA IN PRESENT TIME AMONG ADOLESCENT AND YOUNGER ADULTS IN INDIA.

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***Abstract**: Despite being easily curable and preventive, malaria nonetheless has a terrible effect on people's health and way of life all over the world. Malaria is endemic in India, and the disease predisposes people of all ages to it due to unstable transmission that prevents the immune system from building up. Children under five are the most vulnerable and have the highest mortality rates. This review will examine Indian studies on malaria in both genders. The primary objective of this article is to evaluate scientific data on the proportion of males and females with malaria, as well as statistics on diagnosis, treatment, and primary care settings. The current investigation identified the risk factors for moderate to severe malaria in both men and women, as well as the number of malaria cases in India from 2015 to 2022. We will provide some recommendations for treating malaria and increasing general health at the conclusion of this review.*

Keywords: Malaria, adolescents, pathology, treatment

INTRODUCTION

Malaria, a parasite transmitted by the Anopheles mosquito, is life-threating and poses a major threat to global health. It is transmitted to the humans through the bite of infected female Anopheles mosquitoes, which inject the parasite into the blood stream. The disease is common in places where it is a leading cause of illness and death. malaria is a major public health challenge. Children under five are particularly vulnerable, accounting for around two-thirds of all malaria deaths. Symptoms of malaria often include fever, chills, headache, muscle aches and fatigue. In severe cases, it can lead to anaemia, organ failure, and even death. Malaria also causes complications during pregnancy, including increased risks of maternal and fatal death, low birth weight and infant mortality essential to prevent serious complications and reduce the risk of transmission [1].

Malaria can be treated with a range of antimalarial drug, including artemisinin-based combination therapies which are currently recommended by the World health organization as of the first-line treatment for uncomplicated malaria caused by Plasmodium falciparum. Also, several of preventive measures can be taken to reduce the risk of infection, including the use of mosquitoes. Malaria can also be prevented by chemo prevention or drug prophylaxis before infection occurs. Effects to control and eliminate malaria have been ongoing for many years with the goal of reducing the disease burden and eradicating malaria indefinitely.

Malaria, an acute viral infection primarily transmitted by mosquitoes with life-threatening complications, is one of the most important arthropod-borne diseases of public health concern.

Malaria presents very complex pathophysiological, economic and ecological challenges. Limiting the breeding sites of the vectors that cause morbidity and mortality form these diseases is a public health challenge, although, many areas have not reported malaria for continuous 20 or more consecutive years, and some areas have no known history of the disease. Today, approximately2.5 billion people, or 40% of the world's population live in malaria risk, areas, one of which is at risk of malaria transmission and the regional.

Effort to control and eliminate malaria has been underway for many years, with the goal of reducing the burden of the disease and ultimately eradicating it. Key strategies include vector control, which involves reducing mosquito population through the use of insecticide-treated nets, indoor residual spraying, and other interventions; diagnosis and treatment, which involves ensuring that people with malaria receive prompt and effective treatment to prevent transmission and severe disease [2].

Causative agent: Malaria is a febrile disease caused by the plasmodium parasite, transmitted to humans through the bite of female Anopheles mosquitoes. There are five species of parasites that cause malaria in humans, and two of which are P. falciparum and P. vivax. Plasmodium falciparum is the type of malaria that most often causes severe and life-threating malaria. In the case of malaria, the vector is the Anopheles mosquito and the causative organism is the malaria parasite. Humans and anopheline mosquitoes are both considered to be parasites hosts [2, 3].

Data of malaria 2015-2022 in India: The world health organisation malaria report estimates that there were 241 million malaria cases, including 627,000 deaths, worldwide in2020, which represents around 14 million more cases, and 69,000 more death, than 2019. In India continues to carry the malaria burden for about955 of all cases and 96% of all deaths in 2020, with around 80% of death in the region. Since 2015, the dare for the WHO's global malaria deaths were reported in 24 countries. In The 11 countries with the highest number of malaria cases increase from 150 million in 2015 to 163 million in 2020, and the number of malaria cases decreased by 27.6%, 28.4% in 2019 from 390,000 to 444,600 over that same period. India is the only high endemic country which is reported a decline of 17.6% in 2019 as compared to 2018percentage. The Annual parasitic incidence (API) reduced by 27.6% in 2018 compared to 2017 and by 28.4% in 2019 as compared to 2018. India has API less than once since year 2015.malaria efforts was initiated in the country in2015. Approximately 40 million people in India are infected by mosquitoes each year

Table 1. Year wise cases of malaria

S.no	Year	No of malaria cases in India
1	2015	1,169.26
2	2016	1,087.29
3	2017	844.56
4	2018	429.93
5	2019	338.49
6	2020	186.53
7	2021	161.75
8	2022	46.81

Table 2. Confirmed cases of malaria in male and female

S.no	Sex	positive	Negative	equivocal	total
1	Male	1,120	189	2	1,311
2	female	9,210	153	12	1,045
	Grand total	10,330	342	14	2,356

Main causes of malaria: malaria is caused by a single-celled parasite of the genus plasmodium. The parasite is transmitted to humans most commonly through mosquito bites. Mosquitoes are small flying insects. Female mosquitoes have a long, piercing mouthpiece, with the pierce the skin to consume their blood. Some mosquito bites are harmless. It is only female mosquitos that bite people. Blood serves as a source of protein for their eggs. Male mosquitoes do not consume blood. A person can develop malaria if they receive a bite from an infected mosquito. To cause an infection in a person, the insect must carry a parasite known as Plasmodium. There are many types of this parasite, but humans have only five causes of malaria. Only a bite from a female Anopheles mosquito can transmit malaria to humans. When the mosquito bites a person, the parasite enters the blood. It moves to the liver and begins multiplying. The liver release new malaria parasites back into the blood stream, where they cause infection of red blood cell and multiply further. Some malaria parasites remain in the liver and do not circulate until later, resulting in recurrence. As the parasites multiply, symptoms start to appear, usually 7-30 days after infection, depending on the type of Plasmodium [4]. If a person has an infection after

taking anti-malarial drugs, symptoms may take longer to appear, sometimes weeks or months. An unaffected mosquito could also acquire parasites when it feed on blood containing them which restart the cycle.

Mosquito transmission cycle:

- **Uninfected mosquito:** A mosquito becomes infected by feeding on a person who has malaria.
- **Transmission of parasites:** if this mosquito bites you in the future, it can transmit malaria parasites to you.
- **In the liver:** once the parasites enter your body, they travel to your liver- where some types can lie dormant for as long as a year.
- **Into the bloodstream:** when the parasites mature, they leave the liver and infect your blood cells. This is when people typically develop malaria symptoms.
- **On the next person:** if an uninfected mosquito bite you at this point in the cycle, it will become infected with malaria parasites and can spread them to the other people it bites.

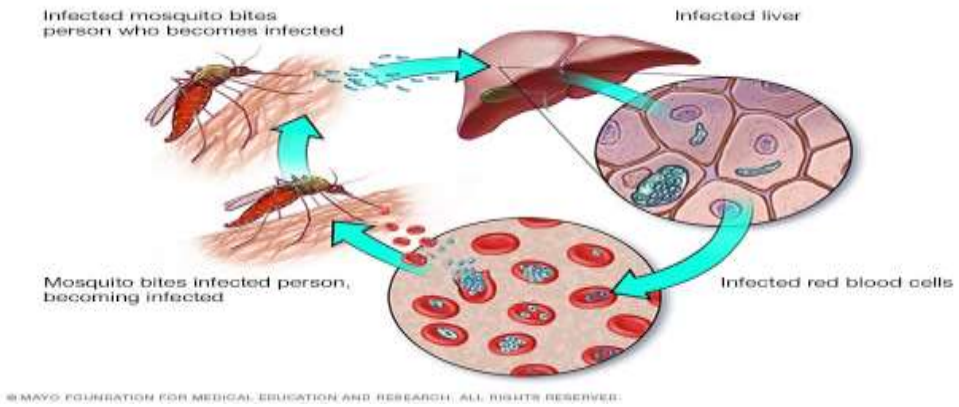


Fig 1. Mosquitoes' transmission cycle

Other mode of transmission: because the parasites that cause malaria affect red blood cell, people can also catch malaria from exposure to infected blood, including.

- From mother to unborn child
- Through blood transfusions
- By sharing needle used to inject drugs

Complications: malaria can be fatal, particularly when caused by the plasmodium species common in India. Malaria deaths are usually related to one or more serious complications, including:

- **Cerebral malaria:** if parasites- filled blood cell block small blood vessel to your brain, swelling of your brain or brain damage may occur. Cerebral malaria may cause seizures and coma
- **Breathing problem:** accumulated fluid in your lungs can make it difficult to breathe.
- **Organ failure:** malaria can damage the kidneys or liver cause the spleen to rupture. any of this condition can be life-threatening.
- **Anaemia:** malaria may result in not having enough red blood cell for an adequate supply of oxygen to your body's tissues.
- **Low blood sugar:** severe forms of malaria can cause low blood sugar, as can quinine-a common medication to use to combat malaria [5].

In Human: Among the parasites of the genus Plasmodium four species have been identified which can cause disease in humans:

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malariae
- Plasmodium knowlesi.

Figure 4. plasmodium falciparum

Scientific classification
Domain: Eukaryota
Phylum: Apicomplexa
Class: Aconoidasida
Order: Haemosporida
Family: Plasmodiidae
Genus: Plasmodium
Species: P. relictum and others of the genus

Treatment: Antimalarial drugs are used for the treatment and prevention of malaria infection. Most antimalarial drug targets the erythrocytic stage of malaria infection, which is the phase of infection that cause symptomatic illness. The extent of pre-erythrocytic activity for most antimalarial drug is not well.
Treatment of the acute blood stage infection is necessary for malaria caused by all species. In addition, for infection due to plasmodium ovale or plasmodium vivax, terminal prophylaxis is required with a drug active against hypnozoites [6].

Antimalarial drug history:

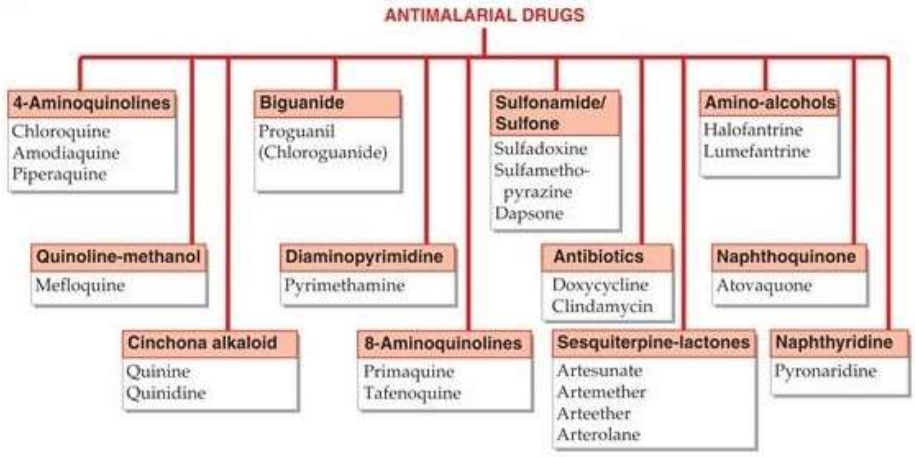
- **17 century-cinchona Tre in Peru**
- **1820 till 1942- cinchona bark**
- **WW I and WW II – java blocked**
- **1926- mepacrine**
- **1945- proguanil**
- **Proguanil, pyrimethamine**

Objective of antimalarial drugs:

- To prevent clinical attack of malaria
- To treat clinical attack of malaria
- To completely eradicate the parasite from patients' body
- To cut down human-to-mosquito transmission

Therapeutic classification [7]:
To prevent clinical attack of malaria (prophylactic):
Causal prophylactics attack the pre-erythrocytic phase in liver which is the cause of malaria infection (tissueschizonticide) **e.g. primaquine, proguanil (100) and atovaquone (250)**
Suppressive prophylactics suppress the erythrocytic phase and prevent attack of malaria fever **e.g., chloroquine, mefloquine, proguanil, doxycycline**
To treat clinical attack of malaria (clinical curative):
Attack the erythrocyte schizonts and terminates episode if malarial fever
(ERYTHROCYTIC SCHIZONTOCIDE)
Fast acting high efficacy ones **(e.g., chloroquine, quinine, artemisinin, mefloquine, halofantrine, lumefantrine, atovaquone**)
Slow acting low efficacy drugs **(e.g., proguanil, pyrimethamine, sulphonamides, tetracycline and clindamycin)**

Classification of antimalarial drug:



Chloroquine (CQ):

- Rapid action **Erythrocytic schizonticide of all species of plasmodium**
- CQ- resistant falciparum
- No effect on primary and secondary hepatic stages and gametes
- Control clinical attack in 1-2 days

Mechanism of action [7, 8]:

haemoglobin → **globin utilized by malarial parasites**

↓

Heme (highly toxic for malaria parasites)

↓

Chloroquine (+) heme polymerase
Quinine,
Mefloquine (-)

Hemozoin (not toxic to plasmodium)

- Plasmodium digest haemoglobin to heme and globin in their vacuole. globin is used by plasmodia for nutrition.
- Heme being's toxic to plasmodium is converted to non-toxic pigment hemozoin by heme polymerase enzyme of the parasites
- Chloroquine concentrates inside the acidic vacuole of parasites and raises the pH of vacuole
- Interferes with conversion of toxic heme to non toxic hemozoin by inhibiting heme polymerase
- CQ- heme complex formed damages plasmodial membranes [9]

Chloroquine resistance [10]

- Chloroquine resistance is fast developing in **P. falciparum** and is a major problem because severe cases of malaria are caused by the species.
- Slow in vivax

- Multidrug resistance- sulfa-pyrimethamine, proguanil, quinine
- Resistance develops due to efflux mechanism

Pharmacological action

- **Antimalarial activity**
- **Other parasitic infection:**
  - Giardiasis, extraintestinal amoebiasis
- **Other action:**
  - Anti-inflammatory, anti-histaminic, local anaesthetic, weak smooth muscle relaxant, anti-arrhythmic activity.

Pharmacokinetics [10, 11, 12]

- Good oral absorption
- Concentrated in liver, spleen, kidney, lungs, skin, leucocytes
- Selective accumulation in retina: ocular toxicity on prolonged use
- T1/2 =3-10 days. Due to tissue binding, small amounts persist in body with terminal t1/2 of 1-2 months

Adverse drug reactions:

Occurring at low dose/ short duration use

- Nausea, vomiting, anorexia, epigastric pain
- Uneasiness
- Uncontrollable itching
- Headache, difficulty in accommodation
- Abortion

Occurring at high dose/ prolonged use

- Loss of hearing
- Mental disturbances
- Rashes, photo allergy

Contraindication

- Liver damage
- Severe GIT, neurological, retinal, hematological disease
- Should not be co– administered with mefloquine, amiodarone, antiarrhythmics
- Can be given in pregnancy
- 250mg oral tablet of chloroquine phosphate consists of 150 mg base

Therapeutic uses

- Giardiasis
- Extraintestinal amoebiasis
- Rheumatoid arthritis
- Discoid lupus Erythematosus
- Lepra reaction
- Infectious mononucleosis

Amodiaquine

- Identical properties to chloroquine
- Less bitter
- Even chloroquine resistant strains may be effective

Piperaquine

- Effective in resistant cases

Mefloquine (quinoline methanol) [13]:

- Developed to deal with chloroquine resistant P. Falciparum
- Rapidly acting erythrocytic schizonticide of chloroquine sensitive and resistant plasmodium (clinical curative)- single dose
- Also, effective suppressive prophylactic for multidrug resistant p. falciparum
- But not gametocidal or kills hypnozoites
- **Mechanism of action similar to chloroquine- relapse**
- **Kinetics:**well, absorbed orally- peak conc.in 5-15 hours
  - Highly bound to plasma protein
  - Conc. In liver, lungs and intestine

- Enterohepatic circulation 2-3 week

Adverse effect:bitter taste, nausea, vomiting, diarrhoea, QT prolongation, neuropsychiatric reaction (ataxia, anxiety, hallucinations)
Uses:in multidrug resistant malaria in combination with ACT- uncomplicated falciparum, CQ resistant and CQ-pyrimethamine resistant.

Quinine

- L- isomer alkaloid isolated from cinchona bark. (Quinine is d-isomer used as antiarrhythmic (mainly) as anti-malarial).
- **Erythrocyte schizonticide** against all plasmodium (including CQ&MDR P. falciparum) but more toxic than CQ and also less effective
  Also kill gametes of p. vivax
  Resistance developed and cross resistance with mefloquine
  Effective in terminating acute attack of falciparum-recrudescence- doxy and clinda
- **Mechanism of action** – similar to chloroquine
- Other action: local irritant and anaesthetic, analgesic, antipyretic and skeletal muscle relaxant

Adverse drug reactions: cinchonism (large single dose / higher therapeutic doses for longer period)

- Tinnitus, nausea and vomiting
- Headache, mental confusion, vertigo, difficulty in hearing and visual disturbances
- Diarrhoea, flushing
- Still higher doses: exaggerated symptoms with delirium, fever, tachypnoea, respiratory depression, pulmonary edema, hypoglycaemia.

Uses

- **Malaria:**
  - Uncomplicated resistant falciparum malaria- oral quinine given – when ACT not available
  - Complicated and severe malaria including cerebral malarial-IV **quinine** DOC
  - Artesunate (IV/IM, artemether (IM), art ether (IM)

Proguanil: Not a popular drug for acute attack (slow action)

Pyrimethamine: directly acting DHFRase inhibitor- high affinity
Used only in the combination with sulphonamide's or dapsone for falciparum malaria treatment.

Sulfoxide-pyrimethamine [13, 14]:

- Long-acting sulphonamides (sulfadoxine)/ dapsone are not effective antimalarial but combination with pyrimethamine causes sequential blockade of folic acid synthesis in plasmodia.
- Slow acting – but combination faster
- Effective against erythrocytic stage of p. falciparum.
- Combination acts faster and prevents development of resistance.
- **Uses:** p. falciparum as curative but not vivax
- Risk of hypersensitivity reaction due to sulphonamide component- SJS, exfoliative- prophylactic dose lesser (pregnancy)

Primaquine [15]:

- Most active against liver hypnozoites (pre-erythrocytic phase).
- Weak action against erythrocytic stage of vivax. No action against erythrocytic stage of falciparum
- Has gametocidal action against all species.
- **MOA**: not known – electron transport

Adverse effect:

- Gastrointestinal
  - Epigastric distress, abdominal cramps,
- Hemopoietic:
  - Mild anaemia, methemoglobinemia, cyanosis, haemolyticanaemia in G6PD deficiency.
- Avoided during pregnancy, G6PD patients

Uses:

- **Primary use is radical cure** of replasing malaria in p. vivax. (15mg daily for 14 days with dose of chloroquine)
- Gametocidal in falciparum malaria (45mg of single dose with chloroquine) &**cut down transmission of malaria.**

Tafenoquine: single dose ant relapse therapy for vivax malaria [16, 17].

Antibiotics:

- Slow but potent action on erythrocytic stage of all antimalarial parasites including multidrug resistance ones.
- Always used in combination with quinine or S-P for treatment of chloroquine resistant malaria.

Halofantrine & lumefantrine [18, 19]:

- Amino alcohol
- Used in chloroquine resistant malaria since 1980
- Now a days used only when no other alternative available

Atovaquone:not used in India

Artemisinin [20]:

- Artemisinin is the active principle of the plant Quinghaosu (artemisia annua)
- Sesquiterpene lactone derivative.
- Lethal to early gametes
- Do not kill primary liver forms of hypnozoites
- Due to short duration of action – high recrudescence rate

Artemisinin derivatives:

- Artemisinin: poorly soluble in water and oil
- **Derivatives:**
- **Artesunate:**in water (oral, IV and IM)
- **Artemether:** in oil (oral and IM)
- Dihydroartemisin'' oral
- **Artemether**: India (in oil and IM)
- **Arterolane**: oral synthetic

Mechanism of action: these compounds have endoperoxide bridge. Heme iron cleaves this endoperoxide bridge to form highly reactive free radicals which damage parasite membrane by covalently binding to membrane proteins [21, 22].

Adverse effects:mild adverse effect life nausea, vomiting, pain, drug fever, itching(common), dizziness, bleeding, leucopoenia is rare.

Uses: uncomplicated p. falciparum and severe and complicated malaria: given parenterally.

Artemisinin based combination therapy (ACT): Artemisinin compound are shorter acting drugs. Monotherapy needs to be extended beyond disappearance of parasite to prevent recrudescence. This can be prevented by combing artemisinin compounds with one long-acting drug life mefloquine etc.

Why combination therapy?

- Rapid clinical and parasitological cur
- High cure rates and low relapse rate
- Absence of resistance

ACT regimens in use [23]:

- Artesunate- sulfadoxine- pyrimethamine
- Artesunate- mefloquine
- Artemether- lumefantrine
- Artesunate- amodiaquine
- Arterolane- piperaquine

Identification test of malaria:

ELISA test: An enzyme-linked immunosorbent assay, also called ELISA or EIA, is a test that detects and measures antibodies in your blood. This test can be used to determine if you have antibodies related to certain infectious conditions. Antibodies are proteins that your body produces in response to harmful substances called antigens. ELISA is often used as a screening tool before more in-depth tests are ordered. A doctor may suggest this test if you're having signs or symptoms of the conditions above. Your doctor may also order this test if they want to rule out any of these conditions [24, 25].

Rapid diagnostic tests: This test helps in detecting the presence of malaria antigens in a blood sample. A testing strip which has malarial antibody is used in this test. A drop of blood is placed in the testing strip and the change in the colour in the strip indicates a positive result. This change of colour is brought about by antigen-antibody reaction. However, this test may not be useful to detect the specific type of Plasmodium which has caused the infection[18].

Blood smear test: A blood smear is a sample of blood that's spread on a glass slide which is treated with a special stain. In the past, all blood smears were examined under a microscope by laboratory professionals. Now automated digital systems may be used to help examine blood smears.
The purpose of examining a blood smear is to check the size, shape, and number of three types of blood cells:

- **Red blood cells**, which carry oxygen from your lungs to the rest of your body
- **White blood cells**, which fight infection
- **Platelets**, which help your blood to clot

Other names: peripheral smear, peripheral blood film, smear, blood film, manual differential, differential slide, blood cell morphology, blood smear analysis [25, 26]

Conclusion: The oldest known human disease is malaria. Although it is preventable, 1–2 million people die from it each year. In this review we conclude that there are several forms of malaria, which proliferate in the liver yet have an impact on the blood. How it affects the blood and its lengthy history. Despite being easily treatable, this illness has claimed the lives of millions of people. The standard for diagnosing malaria is still conventional microscopic examination of peripheral thick and thin blood smears. This procedure is reliable and affordable, albeit it does require a trained microscopest and its sensitivity and specificity differ from those of more recent technological advancements. Here are some preventative steps you may take to manage malaria and halt its future spread.

1. Put on protective gear with long sleeves.
2. Apply insect repellent to any exposed skin by spraying. The suggested repellent comprises 20–35% DEET, also known as N, N-Diethyl-meta-toluamide.
3. If your bedroom doesn't have air conditioning or a screen, use a mosquito net over the bed. You can apply permethrin insecticide to the mosquito net for added security.
4. When you go outside, you can spray bug repellants on your clothing in addition to your exposed skin. Thin clothing is easy for mosquitoes to bite through.
5. Keep your house and surroundings clutter- and waste-free.
6. Watch out for signs like a fever and high temperature. Consult a doctor as soon as you notice any potential malarial symptoms.

References:

1. WHO. World Malaria Report 2015. Available at: http://apps.who. int/iris/bitstream/10665/200018/1/9789241565158_eng.pdf?ua=1. Accessed 24 April 2016.
1. 2.Malaria site, Web portal: http://www.malariasite.com/malaria/Treatment1.htm
2. 3.Wikipedia, The free encyclopedia, Web portal: http://en.wikipedia.org/wiki/Malaria
3. World Health Organization (1958). "Malaria" (PDF). The First Ten Years of the World Health Organization. World Health Organization. pp. 172–87.
4. Sutherland, CJ; Hallett, R (2009). "Detecting malaria parasites outside the blood". J Infect Dis 199 (11): 1561–3
5. Mens, PF; Schoone, GJ; Kager, PA; Schaly, HD (2006). "Detection and identification of human Plasmodium species with real-time quantitative nucleic acid sequence-based amplification". Malaria Journal 5 (80): 80.
6. McCutchan, Thomas F.; Piper, Robert C.; Maker, Michael T. (November 2008). "Use of Malaria Rapid Diagnostic Test to Identify Plasmodium knowlesi Infection". Emerging Infectious Disease (centres for Disease Control) 14 (11): 1750–2
7. Tjitra E, Anstey NM, Sugianto P, Waurika N, Kenangalem E, et al. Multidrug-Resistant Plasmodium vivax Associated with Severe and Fatal Malaria: A Prospective Study in Papua, Indonesia. PLoS Med 2008;5(6): e128.
8. Sarwo Handayani, Daniel T. Chiu, Emiliano Tjitra et al. High Deformability of Plasmodium vivax–Infected Red Blood Cells under Microfluidic Conditions. J. Infect. Dis. 2009
9. J. Alexandra Rowe, Ian G. Handel, Mahammad A. Thera et al. Blood group O protects against severe Plasmodium falciparum malaria through the mechanism of reduced resetting. PNAS 30 October, 2007;104(44):17471-17476.

10. 11.Nicholas M. Anstey, Bruce Russell, Tsing W. Yeo, Ric N. Price. The pathophysiology of vivax malaria. Trends in Parasitology 2009;25(5):220-227.
11. Claire L. Mackintosh, James G. Beeson, Kevin Marsh. Clinical features and pathogenesis of severe malaria. Trends in Parasitology December 2004;20(12):597-603
12. Ian A Clark, Alison C Budd, Lisa M Alleva, William B Cowden. Human malarial disease: a consequence of inflammatory cytokine release. Malaria Journal
13. 14.. WHO. World Malaria Report 2015. Available at: http://apps.who. int/iris/bitstream/10665/2000
14. 15John CJ. Malaria (Plasmodium). In: Kliegman R, Nelson WE, editors. Nelson textbook of Paediatrics, vol. 1. 20th ed. Philadelphia: Elsevier/ Saunders; 2016
15. p. 1709–21. 6. Centre for Disease Control (CDC). Treatment of Malaria (Guidelines for Clinicians). Available at: http://www.cdc. Gov/malaria/diagnosis treatment/clinicians1Accessed 24 April 2016.
16. Phillips A, Bassett P, Szeki S, Newman S, Pasvol G. Risk factors for severe disease in adults with falciparum malaria. Clin Infect Dis. 2009; 48:871–8
17. WHO. Guidelines for treatment of malaria. 3rd edition, 2015. Available at: http://app.who.int/iris/bitstream/10665/162441 /1/9789241549127_eng.pdf?ua=1. Accessed 22 April 2016.
18. Sharma R, Dutta AK. Malaria and National Vector Borne Disease Control Programme. Indian J Paediatric. 2011; 78:1527–35.
19. Gobbi F, Audagnotto S, Trenten L, Nkurunziza I, Coracan M, Di Perri G. Blackwater fever in children, Burundi. Emerge Infect Dis. 2005; 11:1118–20.
20. World Health Organisation. Basic Malaria Microscopy – Part I: Learner's Guide. 2nd edition, February 2010. Available at: http://apps.who.int/iris/bitstream/10665/44208/1/9789241547826_ eng.pdf. Accessed 22 April 2016.
21. Kundu R, Ganguly N, Ghosh TK, Choudhury P, Shah RC. Diagnosis and management of malaria in children: recommendations and IAP plan of action. Indian Paediatric. 2005; 42:1101–14.
22. Gasser RA, Magill AJ, Ruebush T, et al. Malarial Diagnosis: Performance of NOW ®ICT Malaria in a Large-Scale Field Trial [abstract]. In: American Society of Tropical Medicine and Hygiene 54th Annual Meeting; 2005 December 11–15; Washington, DC, USA. (Poster). Am Soc Trop Med Hyg. Abstr 2338.
23. Beadle C, Long GW, Weiss WR, et al. Diagnosis of malaria by detection of P. falciparum HRP II antigen with a rapid dipstick antigen capture assay. Lancet. 1994;343:564–8.
24. Directorate of National Vector Borne Disease Control Programme. Guidelines for Diagnosis and Treatment of Malaria in India 2014. Available at: http://www.mrcindia. Org/Diagnosis%20of%20Malaria%20pdf/Guidelines%202014. pdf. Accessed 24 April 2016.
25. Directorate of National Vector Borne Disease Control Programme. Guidelines for Bivalent RDTS. Available at: http://www.nvbdcp. gov.in/Doc/guidelines-for-bivalent-rdt.pdf. Accessed 24 April 2016.
26. Tripathi KD. Anti-Malarial Drugs. In: Tripathi KD, editor. Essentials of medical pharmacology. 7th ed. New Delhi