PREVALENCE OF CONGENITAL MALARIA AND NEONATAL OUTCOME IN MATERNAL MALARIA IN A TERTIARY CARE CENTRE

Dissertation submitted to

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In partial fulfilment of the regulations for the award of degree of

M.D DEGREE (PEDIATRICS) BRANCH

INSTITUTE OF SOCIAL PEDIATRICS

STANLEY MEDICAL COLLEGE

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DECLARATION

I, **Dr.B.SUBATHRA** solemnly declare that the dissertation titled **"PREVALENCE OF CONGENITAL MALARIA AND NEONATAL OUTCOME IN MATERNAL MALARIA IN A TERTIARY CARE CENTRE"** was done by me at **Government Stanley Medical College during 2014- 2017** under the guidance and supervision of **Prof.S.LAKSHMI M.D, DCH.**

The dissertation is submitted to **The Tamilnadu Dr.M.G.R Medical University** towards the partial fulfilment of the rules and regulations for the **M.D. Degree Examination - BRANCH VII - in Pediatrics**.

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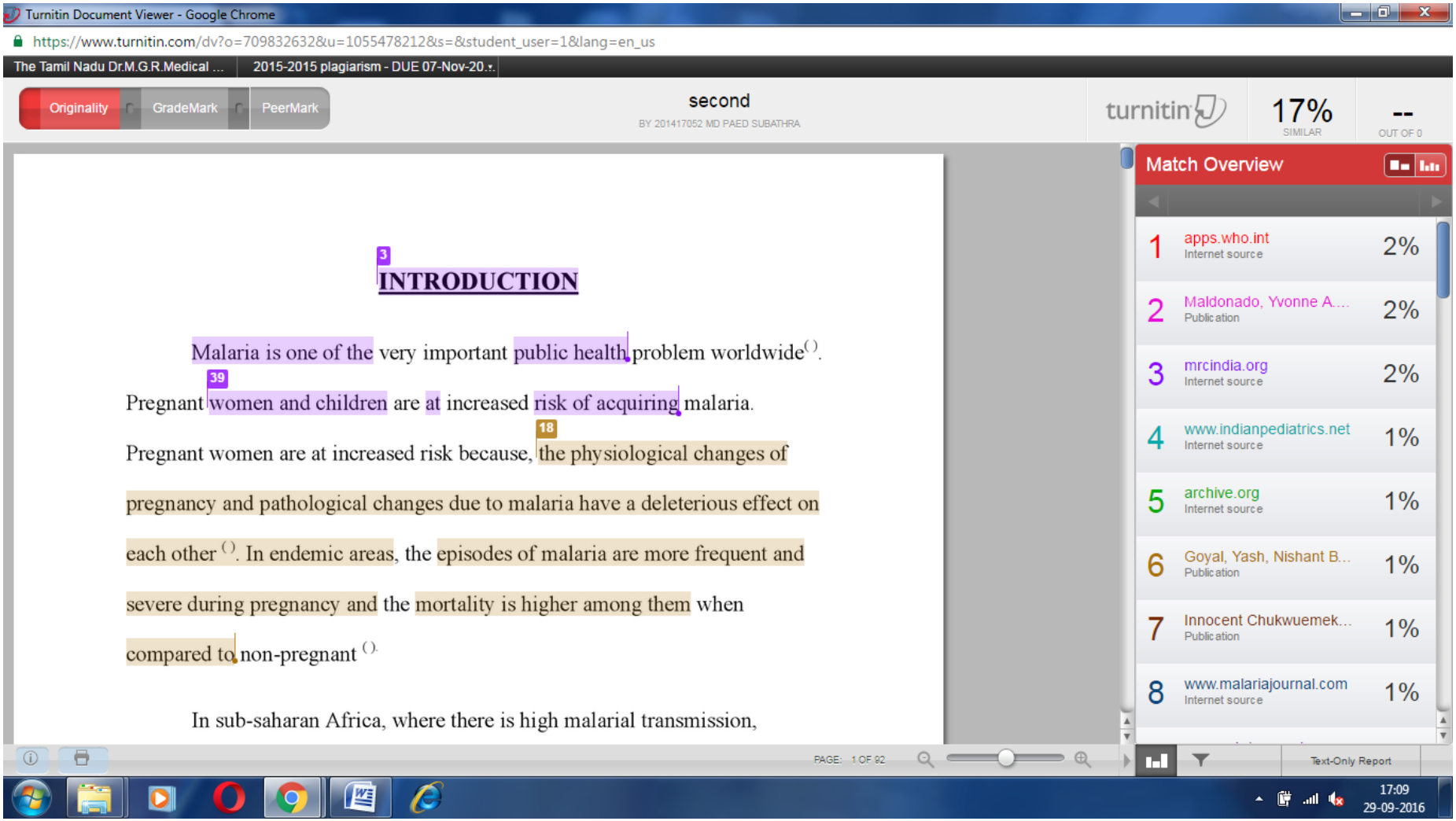
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INTRODUCTION
Malaria is one of the very important public health problem worldwide.
Pregnant women and children are at increased risk of acquiring malaria.
Pregnant women are at increased risk because, the physiological changes of pregnancy and pathological changes due to malaria have a deleterious effect on each other. In endemic areas, the episodes of malaria are more frequent and severe during pregnancy and the mortality is higher among them when compared to non-pregnant.
In sub-saharan Africa, where there is high malarial transmission,
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CONTENTS

INTRODUCTION

Malaria is one of the most important public health problems worldwide [1]. Pregnant women and children are at increased risk of acquiring malaria [2]. Pregnant women are at increased risk because, the physiological changes of pregnancy and pathological changes due to malaria have a deleterious effect on each other [2]. In endemic areas, the episodes of malaria are more frequent and severe during pregnancy and the mortality is higher among pregnant women when compared to non-pregnant [2].

In sub-saharan Africa, where there is high malarial transmission, pregnant women show evidence of peripheral/placental malarial infection at the time of delivery [3]. Women might acquire significant clinical immunity before pregnancy, and placental malaria (i.e malarial parasitemia in the placenta) is often asymptomatic, but can result in maternal anemia and adverse neonatal outcomes [4]. The non-immune primigravida are the most affected [5].

Regardless of the level of endemicity, the main effects of malaria during pregnancy are maternal anemia and low birth weight in the newborn [6, 7, 8] . Malaria in pregnancy can have serious health consequences for both the mother and the infant. It increases the risk of prematurity, low birth weight, maternal anemia and neonatal mortality [5, 9, 10, 11].

Congenital malaria, defined as malarial parasitemia within the first week of life can be acquired transplacentally and is an important consequence of malaria in pregnancy [12]. Congenital malaria was previously thought to be uncommon. However, studies suggest that there is an increase in incidence of congenital malaria observed in both endemic and non-endemic areas [13]. The prevalence in endemic areas has been reported to vary from 0-37 % [14, 15].

Most of these studies were conducted in countries like Africa where the predominant species is Plasmodium falciparum, whereas in India it is P.vivax [16, 17, 18, 19]. In Indian context, there are not many studies to observe the effects of malaria in pregnancy. So, this study was proposed to know the prevalence of congenital malaria and the adverse neonatal outcomes of maternal malaria in our area.

JUSTIFICATION OF THE STUDY

After reviewing various studies, it is known that, pregnant women are at increased risk of getting affected by malaria than the general population. Gestational and placental malaria can cause severe morbidity in both mother and the neonate. Placental malaria increases the risk of maternal anemia, prematurity, low birth weight and neonatal mortality.

Many studies from countries like Africa, have studied in detail the prevalence of gestational, placental and congenital malaria in accordance with the level of malarial transmission. Based on their study results, steps have been taken to reduce the burden of malaria in pregnancy (MiP) in their region.

In Indian context, very few studies have been conducted to find out the effects of malaria in pregnancy. Since the levels of transmission vary from region to region, knowing the effects of malaria in pregnancy in our region, will guide us in taking preventive measures and reduce the burden of malaria in pregnancy.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE:

To determine the prevalence of congenital malaria in a cohort of pregnant women who underwent delivery in our tertiary care centre.

SECONDARY OBJECTIVE:

To assess the neonatal outcome in maternal malaria.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND:

Malaria has existed for over 4000 years. The ancient Chinese medical writings, Nei Ching (the Canon of Medicine), first described the characteristic symptoms of the disease later called as malaria in around 2700 BC. By 4th century, malaria was widely recognised in Greece and was found responsible for the death and decline of most of the city population.

The principal symptoms of malaria were noted by Hippocrates. In the Sanskrit medical treatise (Susruta), the bite of certain insect was attributed as the cause for symptoms in malarial fever [20].

During the second century BC, in China, the Quinghao plant (Artemisia annua), was described in the medical treatise called 52 Remedies. This plant was known as the annual or sweet wormwood in United States.

In 340 BC, Ge Hong of the East Yin Dynasty first described the antifever properties of Quinghao. In 1971, Chinese scientists isolated artemisinin as the active ingredient of Quinghao[20].

In early 17th century, Spanish Jesuit missionaries learned from Indian tribes the usefulness of a medicinal bark to treat fever. The Countess of Chinchon, the wife of the Viceroy of Peru was cured of fever with this bark.

The tree was named Cinchona and the bark was named Peruvian bark. Quinine is the name given to the medicine from the bark [20].

In 1880, a French army surgeon, Charles Louis Alphonse Laveran from Algeria, was the first to identify parasites in the blood of a patient suffering from malaria and named it as Oscillaria malariae [21]. Laveran was awarded Nobel Prize in 1907 for this discovery [21].

An Italian neurophysiologist, Camillo Golgi , in 1886, established two forms of the disease. One with quartan periodicity (every third day fever) and the other with tertian periodicity (every other day fever). He also established that the rupture and release of merozoites in to the blood stream , coincided with the fever episode [20] .

In 1890, the names Plasmodium vivax and Plasmodium malariae for two of the malarial parasites were introduced by the Italian investigators, Giovanni Batista Grassi and Raimondo Filetti. The name Plasmodium falciparum was given to the malignant tertian malarial parasite by William H.Welch, an American. Malarial parasite Plasmodium ovale was described by John William Watson Stephens, in 1992. In 1931, Robert Knowles and Biraj Mohan Das Gupta first described Plasmodium knowlesi [20].

In 1897, August 20th, a British officer, Ronald Ross first demonstrated the transmission of malarial parasite from infected patients to mosquitoes. He

described the sporogonic cycle of malaria transmission. In 1902, Ross was awarded Nobel Prize for his discovery.

In 1899, the complete sporogonic cycle of Plasmodium vivax, Plasmodium falciparum and Plasmodium malariae was demonstrated by a team of Italian investigators.

Hans Andersag, a German, in 1934 discovered Chloroquine and named the compound as Resochin.

In 1946, Chloroquine was finally recognised as a safe and effective antimalarial drug.

THE VECTOR FOR MALARIA:

The female mosquito of the genus Anopheles (fig 1) transmits malaria among humans and acts as a vector. Female mosquitoes take blood meal, to carry out egg production.

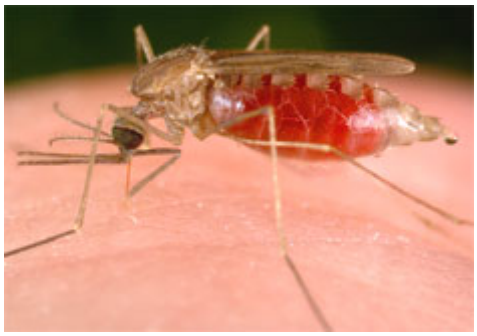

Fig 1 – Anopheles mosquito

ANOPHELES MOSQUITO:

Anopheles is found worldwide except Antarctica. Anopheles gets through four stages in their life cycle as shown in fig 2 [22].

1. Egg
2. Larva
3. Pupa
4. Adult

The first three stages last 5-14 days and are aquatic. They act as malaria vector in adult stage.

EGG: 50-200 eggs are laid per oviposition by adult female mosquitoes. They are laid directly, singly in water. These eggs have floats on their side. Eggs hatch within 2-3 days [22].

LARVAE: Larvae have well developed body, but no legs. In contrast to other mosquitoes, anopheles larvae lack respiratory siphon. The body lies parallel to the surface of water. Larvae prefer unpolluted clean water.

PUPA: When viewed from the side, the pupa is comma-shaped. Like larvae, the pupae must come to the surface to breathe.

ADULT: Adult anopheles has slender bodies with head, thorax and abdomen. The antennae are required to detect host odours and odours of breeding sites

where females lay eggs [22]. To develop from egg to adult, mosquitoes usually take 10 – 14 days in tropical conditions.

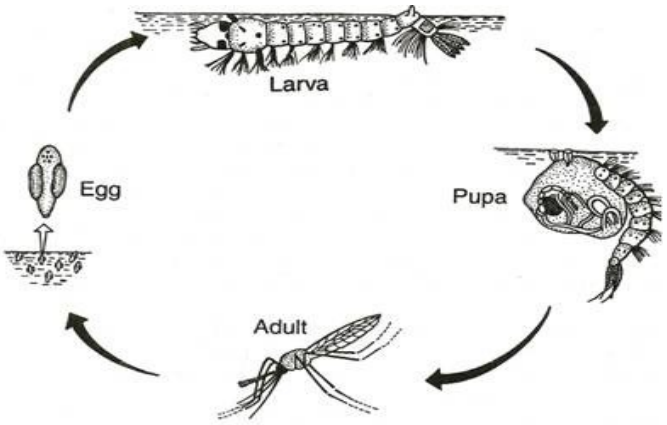

Fig 2 – Life-cycle of Anopheles mosquito

Anopheles can be differentiated from other mosquitoes by the presence of black and white scales on the wings. The typical resting position, with their abdomens sticking up in the air helps to identify the adult anopheles mosquito. Males live for about a week, females live not more than 1-2 weeks.

THE CAUSATIVE AGENT OF MALARIA:

The Plasmodium species are the causative agent of malaria [23]. There are 5 species causing malarial infection:

1. Plasmodium falciparum
2. Plasmodium vivax
3. Plasmodium malariae
4. Plasmodium ovale
5. Plasmodium knowlesi

LIFE CYCLE OF MALARIAL PARASITE:

There are two different host in which malarial parasite passes its lifecycle (fig 3):

1. **In man:** The parasite reproduces by asexual method (schizogony) after residing into the liver cells and the red blood cells. Hence, the intermediate host of malarial parasite is represented by man [24].
2. **In female anopheles mosquito:** The sexual forms (male and female gametocyte) required for the initiation of mosquito cycle is produced inside the human host. The gametocytes are then taken into the mosquito, where they are transformed into sporozoites, which are infective to man. In view of this sexual method of reproduction, the definitive host of malarial parasite is represented by mosquito [24].

HUMAN CYCLE:

The sporozoites are the infective form of the parasite. They are present in the salivary gland of female anopheles mosquito.

When plasmodium species is transmitted by blood transfusion or through placenta, merozoites act as the infective form.

Methods of transmission:

- The main mode of transmission is by inoculative method [25]. During biting, the proboscis of mosquito pierces the skin and the salivary secretions are injected in to the puncture wound. A large number of sporozoites are present in the droplet and are directly introduced in the blood stream.
- Another mode of transmission is trophozoite induced malaria. This type of malaria is induced by injecting blood from a malarial patient which contains the asexual forms of parasite.

The examples of trophozoite induced malaria are as follows:

- Transfusion malaria: When the donor is an infected person, malaria can occur with transfusion of blood from that donor [26, 27].
- Congenital malaria: Infection transmitted to fetus through the placenta in utero [28, 29].
- Malaria in drug addicts: Through using same syringes for many people, when one of them is infected.

After the sporozoites are introduced into human by the bite of an infected female anopheline mosquito. The following stages are present:

1. **Pre-erythrocytic or primary exo-erythrocytic schizogony:**

Sporozoites after entering human body reach the parenchymal cells of the liver to undergo a developmental process. This phase of development is

called as pre-erythrocytic schizogony. This phase consists of only one generation of pre-erythrocytic schizont. The duration of this cycle is 8 days in P.vivax, 9 days in P.ovale and 6 days in P.falciparum.

Many numbers of merozoites are liberated from the schizont. The merozoites that are liberated are called Cryptozoites. The micromerozoites which are smaller ones enter circulation and the macromerozoites which are larger ones, re-enter into the liver cells.

The liver schizonts of P.malariae and P.falciparum rupture once and they do not persist in the liver. Whereas the schizonts of P.vivax and P.ovale can remain dormant in the liver cells for as long as 5 years and can cause relapse of infection.

When the parasites develop inside the liver, there is neither any pathological damage nor any clinical manifestation. During the phase of pre-erythrocytic schizogony, the blood is sterile and the parasites cannot be found in the peripheral blood.

2. Erythrocytic schizogony:

The merozoites produced from the liver by pre-erythrocytic scizogony enter inside the red blood cells. It passes through stages like trophozoite, schizont and merozoite. Once the merozoite enter the erythrocyte, the parasite form ring forms, which enlarge to produce trophozoites. These trophozoites

multiply asexually to produce erythrocytic merozoites which release into the bloodstream when RBCs ruptures.

These parasitic asexual forms can be found in peripheral blood smear 3-4 days after the pre-erythrocytic schizogony is completed i.e 12 days after P.vivax exposure and 9 days after P.falciparum exposure.

The erythrocytic schizogony cycle of P.vivax and P.ovale lasts for about 48-72 hours, and of P.falciparum lasts 48 hours and it is 72 hrs for P.malariae. The clinical attack of malaria is brought about by parasitic multiplication in the erythrocytic phase. The schizogony cycle tends to stop in a course of time either due to spontaneous parasite destruction or due to exhausted capacity of asexual parasites.

3. Gametogony :

After undergoing erythrocytic schozogony, few of the merozoites do not develop in to trophozoites and schizonts. Instead they give rise to forms which are sexually capable after leaving the human host. These forms are called as gametocytes.

Gametocytes develop inside the RBCs present in the capillaries of internal organs (especially spleen and bone marrow). The maturation of this gametocyte is completed in about 96 hours (4days).

In the peripheral blood, only the mature gametocytes can be seen. No febrile episode is caused by these gametocytes. They are necessary for the ultimate continuation of the cycle and propagation of the species. When the individual harbour the gametocytes, they are called ‘carriers’.

4. Latent (hepatic) stage :

In P.falciparum, the pre-erythrocytic schizogony disappears completely after establishing blood infection. Whereas in P.ovale and P.vivax, some of the merozoites persists in the liver cells as dormant forms to produce latent infection. This resting form of parasite is known as hypnozoite.

Hypnozoites are capable of producing merozoites. These latent forms do not arise from the erythrocytic schizogony cycle. These forms are responsible for the relapse caused by P.vivax and P.ovale. Thus, a single infection with P.vivax can persist in the human body, to produce relapse years later.

MOSQUITO CYCLE - SEXUAL CYCLE OF MALARIAL PARASITE:

The human host forms gametocyte that are introduced in to insect host, where it develops further and the sexual cycle is initiated. When a female anopheles mosquito takes blood meal from an infected person, both the asexual and sexual forms of parasites are ingested. But only the sexual forms that are mature can develop further. The rest of the parasite forms die immediately.

A count of atleast 12 gametocyte per mm3 of blood should be present in the blood of human carriers to infect a mosquito. The number of female gametocytes should be more than the number of male gametocytes.

The initial phase of development occurs in the stomach (mid-gut) of the mosquito. About 4-8 thread-like filamentous structures called microgametes develop from one microgametocyte. This developmental process can be seen outside in a moist preparation of blood, so it is called as ex-flagellation. There is no flagellation process in macrogametocyte. Only one macrogamete is produced from one macrogametocyte. The process involved in this maturation includes nuclear reduction and extrusion of polar bodies.

At first, round shaped crescents are formed by the P.falciparum but the remaining process of maturation is same as in other species. The macrogamete attracts the microgamete towards them by the process of chemotaxis and they are ready for the process of fertilization.

The male gamete is attached to the site of small protrusion located in the periphery of the female gamete and penetrates inside their body. After penetration, the male and female pronuclei fuses and a resulting body called zygote is formed. After a mosquito’s blood meal, it takes 20 minutes to 2 hours to form the zygote.

The zygote formed lengthens and mature in to an ookinete, in the next 24 hours. The ookinete was previously called vermicule. The entry of ookinete through the gut wall of the mosquito was explained by Howard in 1906. He suggested that the ookinete was engulfed by the mucosal cell in the gut wall. The mechanism behind this entry was studied by Garnham et al in 1962 using electron microscopy.

The ookinete first comes in contact with a membrane called peritrophic membrane. The barrier is passed and the brush borders of mucosal cells are pushed aside and the anterior end of the ookinete comes close in contact with the host cell membrane. Some proteolytic substances are secreted through a slit present in the anterior end of the ookinete. These proteolytic substances lyse the cell membrane and help the ookinete to enter the cell. Now the ookinete is present in the middle of the cell, and gradually rests against the outer border of the cell and the basement membrane and develops in to an oocyst.

The oocyst is a spherical mass and a structureless capsule surrounds the oocyst. The oocyst contains single vesicular nuclei and a macrogamete pigment granules and it measures 6-12 µm in diameter. Once the maturation starts, the size of the oocyst increases from 6-60 µm. Large numbers of haploid sporozoites are formed after meiotic and mitotic divisions.

Once oocyst fully matures, it ruptures usually on about 10^{th} day of infection, and the sporozoites formed are released in to the body cavity

(haemocele) of the mosquito. The released sporozoites are distributed to various organs and tissues (except ovaries) through the circulating fluid. The sporozoites reach maximum concentration in the salivary ducts, since they have predilection towards the salivary glands.

Once the salivary ducts are filled with sporozoites, the mosquito is capable of transmitting the infection to man. The mosquito can transmit infection with a single bite of human host. Malarial parasite of different species can multiply in the same mosquito and when this infection in transmitted to man, it results in mixed infections, the most common mixed infection being P.vivax and P.falciparum.

INCUBATION PERIOD:

The incubation period of P.vivax, P.falciparum and P.ovale is 10-14 days and for P.malariae it is about 18 days to 6 weeks [21].

SPREAD OF MALARIA:

The following factors are responsible for the spread of malaria:

1. Presence of source of malarial parasite, a gametocyte carrier
2. Existence of an anopheles vector
3. A susceptible person

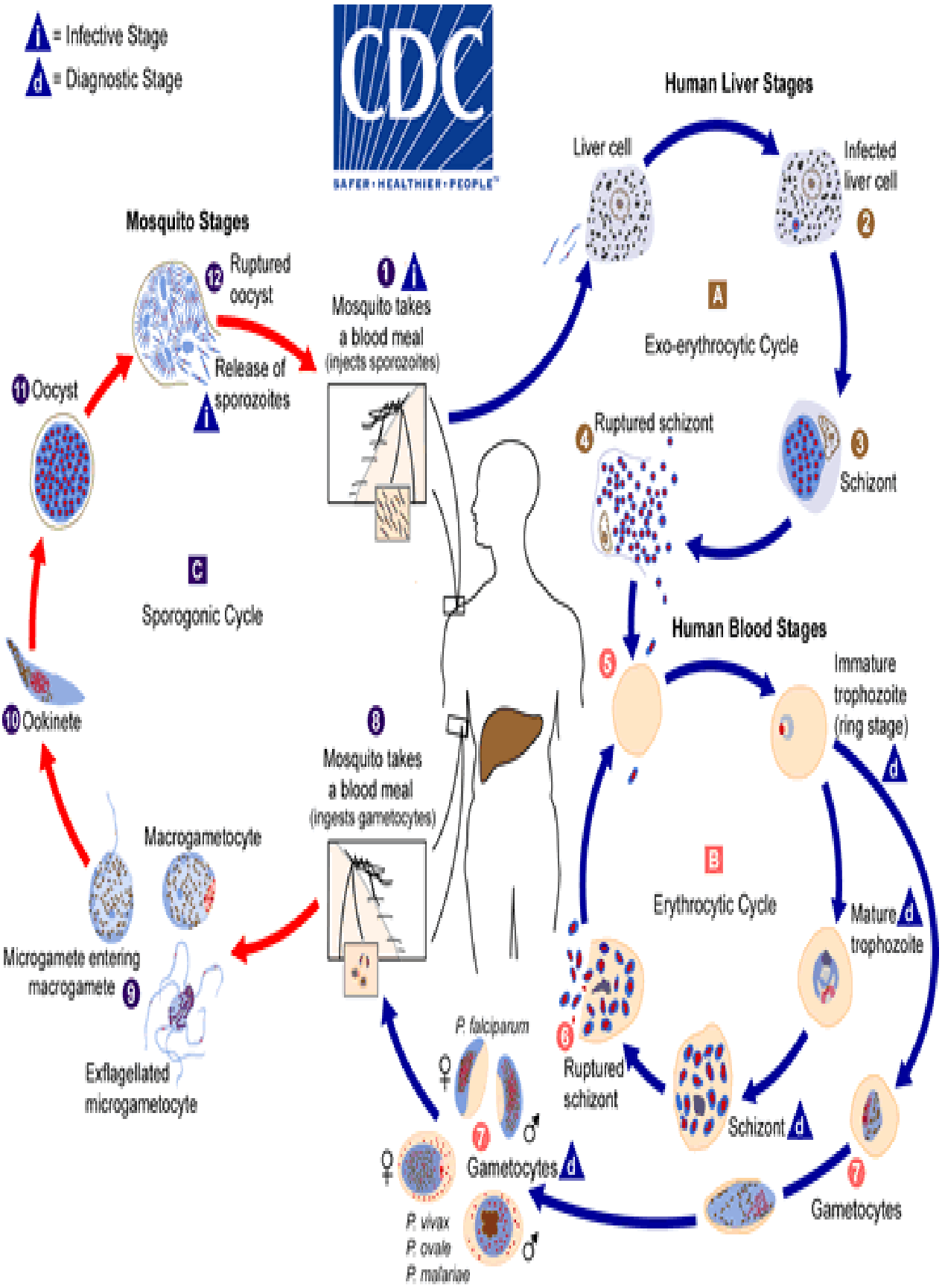

Fig 3 - Life cycle of malarial parasite

ERYTHROCYTE CHANGES IN MALARIA:

After the erythrocytes are invaded, the malarial parasites grow progressively by degrading and consuming the intracellular proteins, mainly haemoglobin [30]. The heme formed which is potentially toxic is converted to malarial pigment (hemozoin) by lipid – mediated crystallization. The parasite changes the transport properties of RBCs, exposes the cryptic surface antigens and inserts the parasite-derived proteins that are newly derived. This alters the RBC membrane making it more irregular in shape, less deformable and more antigenic.

In plasmodium falciparum, 12-15 hours after the cell is invaded, erythrocyte's surface shows membrane protuberances. A high molecular weight, strain specific and antigenically variant erythrocyte membrane adhesive protein (pfEMP 1) extrudes from the knobs [31, 32]. This mediates adhesion of the malarial parasite to the receptors on the venular and capillary endothelium – a process called cytoadhesion. Some of the vascular receptors like intracellular adhesion molecule 1 (ICAM-1) in the brain, CD 36 in many organs and chondroitin sulphate A in the placenta which mediate cytoadhesion have also been identified.

The Plasmodium falciparum infected RBCs attach to uninfected RBCs to form rosettes and agglutinates with other parasitized erythrocytes [33]. The infected erythrocytes also stick inside the vessels and finally block the

capillaries and venules. The cytoadherence, agglutination and resetting are the central processes to the pathogenesis of falciparum malaria [34].

The RBCs containing the mature parasites sequester in the vital organs particularly brain and interfere with metabolism and microcirculatory flow. These sequestered parasites escape the host defence mechanisms especially splenic processing and filtration. Because of the sequestration, only the young ring forms of the parasite can be seen in the peripheral blood and thereby underestimates the true number of parasites present within the body. The infected RBCs are less deformable and are difficult to pass through the obstructed venules and capillaries and thereby have short survival [35].

In all the other three types of human malarias, sequestration does not occur. All stages of development of parasite can be seen in the peripheral blood smear, unlike Plasmodium falciparum. Plasmodium vivax and ovale shows predilection for young RBCs and Plasmodium malariae affects old RBCs. They produce parasitemia which is usually not >2 % whereas Plasmodium falciparum invades RBCs of all ages and are associated with parasitemias of high levels.

PARASITIC ANTIGEN:

The immune response occurs in response to various plasmodial antigens. In infected individuals, the soluble antigen can be detected in the serum by Ouchterlony double diffusion precipitation techniques. The classification of

Plasmodium falciparum antigen based on heat susceptibility was done by Wilson et al. The antigen types are as follows:

(a) A labile antigen (L), which can be destroyed by heating for 30 minutes at 56 c. The two subclasses of L antigen are La (4 antigens) and Lb (3 antigens).

(b) A resistant antigen (R), which is stable at 56 c for 30 minutes.

(c) A stable antigen (S), which is not destroyed even at 100 c for 5 minutes.

HOST RESPONSE:

Initially, nonspecific defence mechanisms are activated by the host in response to plasmodial infection. The immunologic and filtrative clearance functions of the spleen are augmented in malaria. So the removal of both infected and uninfected erythrocytes are accelerated.

The infected cells which escape splenic removal are destroyed during schizont rupture. The macrophages are activated and pro-inflammatory cytokines derived from mononuclear cells are produced in response to the material released during schizont rupture. These cytokines are responsible for fever and other effects occurring after erythrocyte rupture. There can be regular fever patterns like tertian and quartan types.

The presence of some RBC problems like Sickle cell disease, hereditary ovalocytosis, Thalassemias, G6PD deficiency and Haemoglobin C and E provides protection against severe falciparum malaria [36].The decrease in risk of malaria in sickle cell is due to impaired parasite growth at low oxygen tensions. And also the parasitized red cells have reduced cytoadherence.

In α-thalassemia, frequent malarial infection was present in early years of life and thus protected them from severe malarial disease [37]. In Ovalocytosis, the merozoite invasion is resisted by rigid erythrocytes.

The initial non specific host defence mechanisms stop the expansion of infection. The infection is controlled by the later formed strain-specific immune response. Subsequently, exposure to sufficient strains gives protection against high levels of parasitemia and disease and not against infection.

So, in adults and older children living in areas with stable transmission, asymptomatic malaria is common and a state of infection without illness called premunition is present.

Both humoral and cell mediated immunity is produced against malarial parasites. The immunity formed is both species and strain specific. There is an increase in levels of serum IgM, IgA and IgG in immune individuals.

Antibodies produced against the parasitic antigens act by limiting the in vivo replication of the parasites. The most important antigen present in

falciparum malaria is the surface-adhesion protein pfEMP 1. The antibodies passively transferred from the immune adults to children resulted in reduced parasitemia in children. The transfer of antibodies from mother has resulted in less severe infections in infants in the first few months of life. If the person lives outside the endemic area for longer duration, this protective immunity decreases.

The cellulo-humoral defence mechanism of the host against the parasite is effective only against the asexual erythrocyte parasites. It is not effective against the hypnozoit and the gametocytes. So even in the absence of re-infection, the merozoites released from the latent phase of hepatic cycle enter the RBCs and cause a clinical attack of malaria.

If the immune mechanism in effective, the merozoites released by the schizonts in the liver can be destroyed, thereby preventing a clinical attack. The released merozoites can invade the erythrocytes only when the immune mechanism fails.

CLINICAL FEATURES OF MALARIA:

1. **Febrile paroxyms:** Fever is one of the cardinal symptoms present in malaria. It can be continuous or intermittent. It can be associated with chills and rigor. There are 3 stages in febrile paroxysm of malaria [38, 39, 40] :

   A) The cold stage (may last for about 20 minutes to an hour)

B) The hot stage (lasting between 1 to 4 hours)

C) The sweating stage (lasting between 2 to 3 hours)

The total duration of febrile period lasts from 6-10 hours. The febrile paroxysms occur in synchrony with the erythrocytic schizogony phase of the malarial parasite.

- The fever recurs every third day with a 48 hour cycle called tertian fever. This type is caused by P.vivax
- The fever recurs every fourth day with a 72 hour cycle called a quartan fever. This type is caused by P.malariae

The fever is usually accompanied by myalgia, anorexia, headache, nausea, vomiting and arthralgia. The symptoms can be non-specific mimicing other diseases like enteric fever, common viral infections etc.

1. **Anemia:** During segmentation of parasites, the RBCs breakdown resulting in microcytic hypochromic anemia [40] .
2. **Splenomegaly:** One of the most important physical signs in malaria is enlargement of spleen. After few paroxysms, usually by the end of 2nd week it is enlarged and palpable [39] .

Malaria should be suspected in people living in endemic areas and in those who present with above symptoms and signs. It should be suspected in individuals who have visited an endemic area recently.

COMPLICATIONS OF PLASMODIUM FALCIPARUM MALARIA:

The 10 complications of malaria that define severe malaria have been identified by world health organisation [38, 41]. They are as follows:

1. **Impaired consciousness:** A Blantyre coma score of < 3 in children or a Glasgow coma score of < 11 in adults.
2. **Prostration :** Generalised weakness making the person to need assistance to sit, stand or walk.
3. **Multiple convulsions:** 2 or more episodes of seizures within a 24 hour period. Usually occurs with cerebral malaria. The standard medications used for treatment are phenobarbitone or phenytoin.
4. **Acidosis :** A base deficit of >8meq/l or a plasma bicarbonate of < 15 mmol/l. Severe acidosis clinically manifests as respiratory distress. It has a poor prognostic indicator in severe malaria.
5. **Hypoglcaemia :** Blood or plasma glucose levels < 40 mg/dl. Hypoglycaemia is more common in pregnant women, children and patients who have received quinine therapy. Children resent with altered level of consciousness that is usually confused with cerebral malaria.
6. **Severe malarial anemia :** In children < 12 years, Haemoglobin concentration of < 5g/dl or a haematocrit of < 15 % with a parasite count > 10,000 /µl. Anemia is the most sever complication of malaria among children than hemolysis. Removal of erythrocytes that are infected by the

spleen and impairment of erythropoiesis play a major role in the pathogenesis of anemia in malaria.

7. **Renal impairment :** Serum creatinine levels > 3 mg/dl or blood urea > 20 mmol/l
8. **Jaundice :** Serum bilirubin > 3 mg/dl with a parasite count of > 100000/ul
9. **Pulmonary oedema:** Oxygen saturation < 92 % or radiologically confirmed pulmonary edema with respiratory rate > 30/minute, usually associated with chest retractions, crepitations on auscultation.
10. **Significant bleeding :** Prolonged or recurrent bleeding from gums, nose etc
11. **Shock :** Compensated shock is defined as impaired perfusion with capillary refill > 3 sec, but there is no hypotension. Decompensated shock is evidence of impaired perfusion with hypotension.
12. **Hyperparasitemia :** P.falciparum parasitemia > 10 %

OTHER COMPLICATIONS OF P.FALCIPARUM MALARIA:

1. Cerebral malaria:

- Cerebral malaria is defined as the presence of coma in a child with Plasmodium falciparum parasitemia and the absence of other causes for coma.
- Due to rosetting of sequestered parasitized RBCs, there is plugging of capillaries in the brain that leads to vascular occlusion and cerebral anoxia [42].

- Although trophozoites and schizonts are the common forms identified in brain capillaries, gametocytes have also been observed.
- In about 50% of children and 10% of adults, cerebral malaria manifests with generalised convulsions and symmetrical encephalopathy.
- Cerebral malaria is common in areas of midlevel transmission. But it is less frequent in areas with very high transmission.
- Physical findings [39]:
    - High fever
    - Seizures
    - Rhythmic movements
    - Muscular twitching
    - Unequal pupils
    - Hemiplegia
    - Deep tendon reflexes that are absent or exaggerated
    - Positive babinski sign
- Signs of meningeal irritation and focal deficits are usually absent.
- Studies show that fundoscopic findings like retinal hemmorhages, macular whitening and vessel changes suggestive of malarial retinopathy are specific for cerebral malaria.
- Mortality rate is about 15 % in children and 20 % in adults.

2. Pernicious anemia:

This constitutes blackwater fever, algid malaria and septicemic malaria.

3. Black water fever:

- This fever is characterised by fever, dark urine and hemoglobinuria due to sudden intravascular hemolysis.
- The exact mechanism behind blackwater fever is not known. This usually occurs in patients infected with falciparum following quinine treatment.
- Few autoimmune mechanisms have been proposed. Antibodies develop against the quininised and parasitized RBCs. So with subsequent quinine treatment there is immune complex formation and complement mediated destruction of the RBCs leading to the manifestations of blackwater fever.

4. Algid malaria:

Algid malaria is a rare complication that manifests with hypothermia, hypotension, shallow breathing, weak pulse, peripheral circulatory failure and profound shock.

5. Septicemic malaria:

This type is characterised by high grade fever with sequestration of parasites in various organs leading to multiorgan failure.

6. **Tropical splenomegaly syndrome:** (hyperactive malarial splenomegaly)

- This occurs more commonly in malaria endemic areas
- This is a chronic complication following P.falciparum malaria, in which there is massive splenomegaly that persists even after the treatment of acute infection.
- This results from abnormal immunological response to falciparum antigens.
- It is characterised by massive splenomegaly, hepatomegaly and elevated IgM level of antibodies.
- Prolonged antimalarial prophylaxis is required to treat the syndrome.

MALARIA AND PREGNANCY:

Malarial infection in pregnancy is a social, medical and obstetric problem that should be treated in a multidisciplinary approach [1]. The main adult risk group for malaria are pregnant women. In Africa, pregnant women constitute 80% of deaths due to malaria.

Pregnancy and malaria mutually aggravate each other. The physiological changes in pregnancy are synergistic with the pathological changes occurring due to malarial infection [2]. In pregnant women, Plasmodium falciparum can have a dramatic and turbulent course. Primigravidae who are non-immune are the most affected groups [5].

The morbidities that can occur in pregnant women due to malaria are anemia, febrile illness, cerebral malaria, hypoglycaemia, puerperal sepsis, pulmonary edema and maternal mortality. Mortality is mainly due to hemorrhage and severe malaria. The neonatal outcomes can be prematurity, low birth weight, intrauterine growth retardation and mortality [6].

EFFECTS OF PREGNANCY ON MALARIA:

Pregnant women have increased density and prevalence of malarial parasitemia than non pregnant women who reside in similar geographical area [43, 44, 45, 46, 47].

A Plasmodium falciparum parasitemia of 6896/mm3 in pregnant women and 3808/mm3 in non-pregnant women and Plasmodium vivax parasite density of 3564/mm3 in pregnant women and 1949/mm3 in non-pregnant women was found by Campbell and colleagues [48].

Reinhardt and associates found that primiparity were much more affected than higher parity. With increase in parity, the prevalence and density of parasitemia decreased. This decrease in prevalence is explained by an increase in immunity that occurs with increase in age.

This concludes that both pregnancy and age are important determinants of infection susceptibility [43, 44, 45].

MALARIA AND PREGNANCY- DOUBLE TROUBLE:

- Pregnant women are more commonly affected by malaria than the general population. Loss of acquired immunity and immunosuppression could be possible causes.
- The hormonal, haematological and immunological changes in pregnancy make malaria present atypically in pregnant women [43].
- Due to immunological changes, parasitemia is higher in pregnant women and so malaria tends to be more severe than the non-pregnant women.
- The severity of malaria increases, which turns out to be fatal too. The mortality rate is high in pregnant when compared to the non-pregnant population.
- Treating malaria in pregnant women becomes difficult, in view of contraindication and adverse effects of some antimalarials.
- Complications of malaria in pregnancy are difficult to manage.

PATHOPHYSIOLOGY:

The presence of a new organ named placenta in pregnancy and altered immune status contributes greatly to the pathophysiology of malaria in pregnancy. The hypotheses that explain the pathophysiology of malaria in pregnancy are as follows:

- Elevated serum cortisol levels reduce lymporoliferative response with a general immunosupression and reduced antimalarial immunity. However, the diminished susceptibility to malaria by multigravidae women cannot be explained by this hypothesis [49].
- In primigravida, placenta is a new organ and allows the parasites to bypass the host immunity and thereby allows multiplication of placenta specific plasmodium species. In multigravida, placenta specific immunity is developed, which explains the diminished susceptibility to malarial infection.
- In pregnancy, there is a bias in immunity towards type-2 cytokines and are therefore susceptible to disease like malaria, tuberculosis, Leishmaniasis which requires type 1 response for protection. However, a change in local placental immunity from Th2 response to Th1 response has been observed in infected pregnant women [50].

This is supported by the evidence that, there are elevated levels of hallmarks of type 1 cytokine response like TNF-α, INF-γ, and IL-2, while IL-10 levels are decreased.

Severe maternal anemia, symptoms of malaria is contributed by elevated levels of TNF-α. Localised cytokine elevation in the placenta contributes much to the adverse neonatal outcome.

PLACENTA – A NEW ORGAN IN PREGNANCY:

Cytoadhesion is a unique ability of Plasmodium falciparum. The adhesion molecules like intercellular adhesion molecule-1 and CD 36 play a role in malarial infection of non- pregnant adults and children. In pregnancy, the adhesion molecules for parasite adhesion to placenta are hyaluronic acid and chondroitin sulphate A [35].

The placental membranes are sequestered by parasites especially along the extravillous trophoblasts, tropoblastic villi and syncytial bridges. The macrophages and parasites occupy the intervillous space. There is villous hypertrophy and fibrinoid necrosis of the villi. All these changes contribute to the decrease in transport of oxygen and nutrients from the mother to the fetus through the placenta. There is generalised hemorrhaging and pigment formation in the placental tissues.

MALARIAL INFECTION AND INTENSITY OF TRANSMISSION:

Depending on the level of transmission in an area, the severity and clinical presentation of the disease in pregnancy differs due to the difference in the immunity level.

In high endemic and high transmission areas, the acquired immunity is high and so the presence of asymptomatic and incidental parasitemia is common [4]. The mortality is low. The peripheral blood can be negative for malarial

parasite, but the sequestration of parasite in placenta can cause long standing placental malaria. This altered placental integrity results in adverse outcomes like low birth weight, stillbirth and prematurity. And these effects are more common in the first and second pregnancy when compared to higher gravida. HIV infection and further immune suppression makes the pregnant women even more susceptible to malarial infections.

In low transmission areas, the risk of infection with malaria is higher. The risk of spontaneous abortion and maternal death is also high. Asymptomatic malaria is rare [6].

MANIFESTATIONS OF MALARIA IN PREGNANCY:

Atypical infections are common in pregnancy, particularly in the second half of pregnancy.

1. Fever
2. Anemia
3. Splenomegaly

COMPLICATIONS OF MALARIA IN PREGNANCY:

1. Anemia: Anemia in pregnancy can be caused or aggravated by malaria [46]. It could be due to,
    - High pregnancy demands
    - Hemolysis of parasitized RBCs

- With higher parasitemia, anemia can be more severe. Anemia increases maternal and perinatal mortality.

2. Acute pulmonary edema:

   This is a more common complication in pregnancy than non pregnant population. It is more common in second or third trimesters. It can present suddenly in the immediate postpartum period, due to high amount of parasitized RBCs entering the circulation from the placenta. This aggravates the pre-existing anemia.

3. Hypoglycaemia
4. Immune suppression:

   Hormonal and immunological changes cause immunosuppression in pregnancy. In addition malaria by itself suppress immune respone. So these women are more at risk of other secondary infections.

5. Renal failure

EFFECT OF MALARIA ON FETAL SURVIVAL AND BIRTH WEIGHT:

About 40% of pregnant women in the world are exposed to infection with malaria during pregnancy. Malaria can be associated with increased risk of perinatal and maternal mortality if there is little or no previous immunity. In non immune pregnant women with malaria, fetal loss has been high [51]. Many women sustain spontaneous abortions when infected during the first trimester.

Infection of the placenta with parasites resulted in more low birth weight than when the mother was infected, but placenta was not [44, 45, 52, 53, 54]. The mean birth weight was more when the placenta was infected with Plasmodium falciparum than being infected with Plasmodium vivax. The fetus is affected due to maternal anemia and placental insufficiency.

It is postulated that, the circulation of maternal blood through the placenta is interfered by infiltration of lymphocytes, macrophages and parasites in the placenta. This resulted in decreased oxygen and nutrient transport to the fetus [45].When placental inflammation was severe, the transport of antibodies to malaria through the placenta was also decreased [43].

Bruce-Chwatt [55] found that the infant birth weight was less when the placenta was infected compared to uninfected placenta. And the same was proved by Archibald et al [56]. Infants who had demonstrable cord blood parasites at the time of delivery were more affected than who did not have parasitemia.

Using the gestational age scoring system developed by dubowitz and associates [57], Reinhardt and colleagues [44] found that there was no evidence of increase in incidence of small for gestational age infants, when the placenta was infected. This suggests that prematurity resulted in low birth weight in infants born to women with malaria.

Jelliffe [52] in his study demonstrated on indirect effect of malaria on infant survival in endemic countries. This was further supported by Macgregor and Avery [58] that malaria control in a region resulted in increase in birth weight of infants born in that region.

It is demonstrated that malarial infection in the first half of pregnancy results in decreased fetal growth than in the third trimester.

Therefore, malaria contributes to fetal loss, low birth weight, still birth, prematurity and neonatal mortality [54, 59].

INFLUENCE OF MATERNAL ANTIBODIES ON INFECTION RISK:

Antibodies against malaria are transferred from mother to infant through the placenta. Bray and Anderson suggested that, heavy infiltration of parasites in the placenta resulted in decrease in the amount of IgG transferred to the fetus.

Malarial antibodies can be detected by indirect hemagglutination, complement fixation and indirect fluorescence method. Both agglutinating and precipitating antibodies are also formed [60].

The amount of antibodies by indirect hemagglutination decreased from birth till 25 weeks of age [61, 62]. But endogenous antibody levels increased as a result of postnatal exposure to infection.

CONGENITAL MALARIA:

There are no consistently accepted definitions for congenital malaria. Some accept demonstrating parasites in the peripheral blood on first day of life. Some accept cases that were confirmed within first 7 days of life [59]. It is difficult to distinguish between congenital malaria and acquired cases, since infants are exposed to mosquitoes at a very young age in malaria endemic regions. However, many cases of congenital malaria have been reported from countries free from malaria.

The antibodies transmitted from the mother to the fetus are an important factor that determines whether the parasite that reach fetal circulation establishes an infection or not. The placental infection frequency differs according to the prevalence of malaria in the region, availability of antimalarial drugs and the vigor of measure of control. Despite involvement of placenta, clinically apparent congenital infections remains rare in areas where malaria is endemic and maternal immunity levels are high.

The presence of congenital malaria was more in infants born to women who had clinical malarial attacks during pregnancy than those with chronic infections that were subclinical. Still, congenital malaria can occur in infants of women who were asymptomatic throughout their pregnancy [59, 63, 64].

Evident parasitemia is mostly not demonstrable in the mother [65]. Congenital malaria is more common in infants born to women who have immigrated to malaria endemic areas, than who have been raised in the same area, because of low levels of immunity than the native population.

CLINICAL PRESENTATIONS:

Congenital malaria cases have been identified in malaria endemic countries than the non endemic ones. The onset of first symptom or sign occurred when infant was 10-28 days of age [66, 67, 68]. However, it can occur as early as 8 hours to as late as 8 weeks of age. No association has been found between plasmodium species and the age of onset of symptoms. Most congenital infections occurred when mother suffered a clinical attack of malaria during pregnancy.

In more than 80% of cases, clinical findings most commonly found were fever, anemia and splenomegaly [66, 69]. Anemia was associated with reticulocytosis in most of the cases. Hyperbilirubinemia and jaundice have been identified in some cases.

Depending on the process, whether liver dysfunction or hemolysis, the direct or indirect bilirubin levels may be elevated [66]. Hepatomegaly can occur but is less likely than splenomegaly. Failure to thrive, loose stools and regurgitation can be the presenting findings.

DIAGNOSIS:

1. Examination of peripheral blood smear for parasites:

The gold standard method of detecting malarial parasite is examining blood smear stained with Giemsa or Wright stain.

Collection of sample:

The ideal specimen to look for malarial parasite is in a blood taken directly from a finger prick. Because this method gives the best staining characteristics. Blood collected in Ethylene diamine tetracetic acid (EDTA) should be processed within 1 hour. If the processing time is more than 1 hour, distortion of the organisms can occur. If the time exceeds 4 hours, organisms may be lost [70].

If stained with Giemsa stain, the chromatin stains red or purple red and the parasite's cytoplasm stains blue. If malarial stippling is present, it is seen as discrete pink-red dots. The best morphology picture of parasite can be obtained when stained with Giemsa. But the procedure is time consuming. If stained with Wright stain, the colour intensity to differentiate the parasite is not as good as Giemsa stain. But staining with Wright stain takes only short duration.

Identification procedure:

To detect blood parasites, two smears should be made. One thick film and another thin film. The preparation method of both films is different and

therefore should be done in two different slides. They can be stained with any one of the Romanowskys stain such as Giemsa and Field's, Leishman's, Wright's or Jaswant Singh and Bhattacharya (JSB) stain. The best staining of organisms in both thick and thin film is done by Giemsa stain [70].

Thick film:

A thick film has high sensitivity and it is best for the detection of malarial parasites. This is because of the fact that organisms in large volume of blood concentrate in a relatively small area.

A thick film is made after several drops of blood is pooled and spreading it into an area of 1.5 cm. An optimal thickness is present, when newsprint is visible barely through the blood drop before it is dried. There is peeling from the slide if the film is too thick.

Before staining, the film should be dried for 6 hours. Fixing a slide prevents lysis of red blood cells. So, thick film should not be fixed before staining. Giemsa staining causes lysis of unfixed RBCs and release hemoglobin. To detect malarial parasites, thick film is examined at *1000 [71, 72].

In the thick film, only platelets, parasites and white blood cells are present because the RBCs are destroyed. Comparing the size of infected and non-infected erythrocytes cannot be done in a thick film.

Thin film:

For making thin film, a drop of blood should be taken in the corner of the slide. Another slide at 45 degree angle is used to spread by and then it is pushed gently to the lift, till the blood is over. The thin film should be air dried for 1 minute. Then it is stained with Giemsa stain.

Good thin film surface should be:

1. Uniform and even.
2. RBCs should be in a single layer.
3. The tail end should be near the centre of the slide.
4. Margins of the film should not extend the sides of the slide.

It is then examined under oil immersion field to look for parasites. If malaria is suspected, several samples from the patient over 36-48 hours should be examined, before giving a negative final report. The parasite characteristics and RBCs can be seen in a thin film. So it is used for species identification. The percentage of erythrocytes parasitized (parasitemia) is calculated from thin blood smear.

Identification of different malarial species:

1. **Plasmodium vivax:** P.vivax takes 48 hours for its life cycle to be completed. This is a tertian life cycle pattern. The new group of RBCs are invaded every third day. P.vivax invades young RBCs usually.

- It is characterised by enlarged infected RBCs, usually up to double the size.
- Schuffners stippling (a fine pink stippling) may be present in the cell.
- Ameboid appearance characteristic of young trophozoites are present
- After maturity, RBCs is filled and golden brown pigment is present
- About 12-24 merozoites are present in mature schizont, with an average of 16.
- Gametocytes appear round and fill the cell.

2. **Plasmodium malariae**: P.malariae takes 72 hours for its life cycle to be completed. This is a quartan life cycle pattern. The new group of RBCs are invaded every fourth day. P.malariae invades older RBCs usually.

- Band appearance is characteristic of trophozoites, and it is stretched across the RBCs diameter. The dark, coarse, brown black pigment can be seen in band form.
- Pink cytoplasmic dots named Ziemanns dots can be seen.
- About 6 -12 merozoites are present in a mature schizont, with an average of 8.
- Merozoites are arranged around the clumped pigment and the characteristic “loose daisy petal” arrangement can be seen. They can be arranged randomly also.

3. **Plasmodium ovale:** P.ovale is the less commonly seen species. It resembles P.vivax and exhibits a tertian life cycle pattern.

- The infected RBCs are enlarged and oval shape is assumed with fringelike or fimbriated edges.
- Schuffners dots can be present but less common than P.vivax.
- The parasites have golden brown pigment and remain compact.
- About 6-12 merozoites are present in a mature schizont.

4. **Plasmodium falciparum**: The life cycle of P.falciparum is asynchronous and the RBCs rupture at irregular intervals ranging from 36-48 hours. Only the ring for trophozoites and gametocyte can be seen in the peripheral blood of P.falciparum. The rest stages are present in the capillaries and venules of major organs. RBCs of any age are invaded by P.falciparum, so it exhibits the highest parasitemia among all infected patients.

The ring forms of P.falciparum exhibits two chromatin dots [72]:

- Appliqué forms in which parasites are seen at the edge of the RBCs and multiple ring forms are seen in a single RBC.
- Occasionally, Maurer dots, small comma-shaped red dots are seen in the cytoplasm of the infected cells.
- The mature trophozoite is compact and small.
- The dark brown pigment is present in the mature trophozoites.

- About 8-36 merozoites are present in a mature schizont, with an average of 20-24.
- Gametocyte show characteristic crescent or banana shape.

Advantages of peripheral smear examination:

1. Peripheral smear is cheap
2. Thick smear is about 40 times more sensitive than thin film. It can detect a parasite density of even 5-10 parasites/µl.
3. Parasite quantification can be done.
4. Thin smear can be used to specify the malarial species.
5. Malaria pigment can be demonstrated in a smear.

Disadvantages:

1. Procedure is labour intensive
2. Experienced technician is required.
3. Low sensitivity. Thin film requires >200 parasites/µl of blood to detect parasites.

2. RAPID DIAGNOSTIC TEST: (RDT)

Malaria is a curable disease if diagnosed early and treated promptly. Rapid diagnostic test (RDT) that are antigen based have a major role in diagnosing malaria especially in areas that lack microscopes and trained technicians to identify parasites in blood films. These are based on lateral flow

assay called Immunochromatographic test that capture parasitic antigens from the blood either by using a monoclonal or polyclonal antibodies against the parasitic antigens.

The first malarial antigen used as target was a soluble glycolytic enzyme glutamate dehydrogenase [73, 74, 75]. The antigens that can be targeted by immunochromatographic tests are Histidine-rich protein 2 of P.falciparum, plasmodium Aldolase of all malarial parasites and Lactate dehydrogenase that are specific to malarial parasite. The RDTs are simple to perform as they do not require electricity, laboratory or any specific equipment.

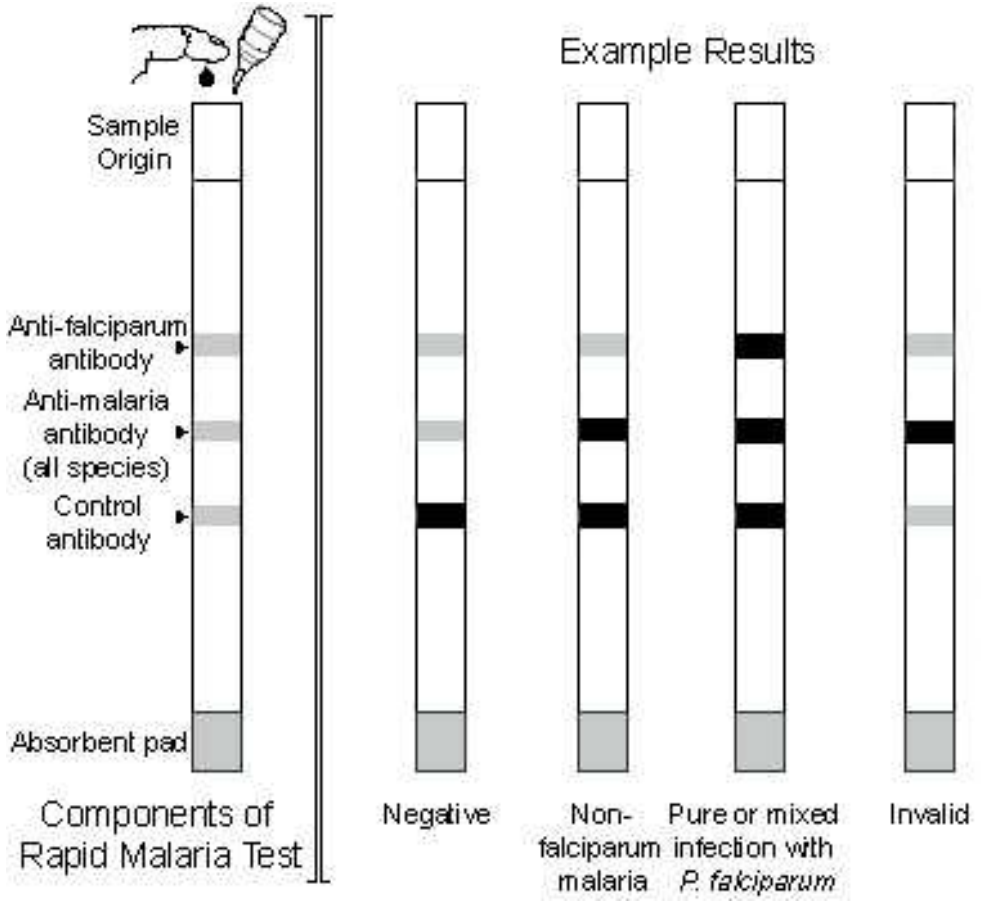

Fig 4 – Rapid Diagnostic Test

1. Histidine rich protein 2 of P.falciparum (HRP-2):

HRP-2 is a alanine and histidine rich, water soluble protein, that is localised in the parasitic cytoplasm. This antigen is expressed only by the trophozoites and young gametocytes of P.falciparum [76, 77]. An adequate amount of HRP-2 is secreted in the blood stream of the host by the parasite and it is detected in the serum, plasma, erythrocytes, CSF, urine as a water soluble protein [78]. This antigen persists in the blood even after the parasitemia has been reduced or cleared. It takes around 3-4 weeks for the HRP-2 test to turn negative after successful treatment [79].

2. Parasite Lactate dehydrogenase (pLDH):

pLDH is a soluble glycolytic enzyme. This is the last enzyme present in the glycolytic pathway that is essential for ATP production [80]. This enzyme is produced by both sexual and asexual stages of the live parasite and it is released from the erythrocytes that are infected by the parasites. All 4 species of malaria releases this enzyme and species isomers of pLDH for 4 species exist. The blood levels of pLDH reduce faster than the levels of HRP-2 after treatment [81].

3. Plasmodium Aldolase (pAldo):

pAldo is an enzyme involved in the glycolytic pathway of parasites and it is produced by the blood stages of both non-falciparum malarial parasites and P.falciparum [82].

The rapid malarial tests:

There are various test formats to perform RDTs like strip, card, dipstick or cassette. The testing procedure varies between each test kit. The blood specimen required to perform the procedure is a finger-prick blood specimen, plasma or anticoagulated blood , that is mixed with a buffer solution that contain a hemolyzing compound.

There are specific antibodies that are labelled with a detectable marker that can be visualised such as colloidal gold. In few kits, there is a pre-deposited labelled antibody and a washing/lysing buffer is added.

If the antigen that is targeted is present in the blood, it migrates through the nitro-cellulose membrane by capillary action in the test strip and it is captured by the pre-deposited antibodies that are specific against the antigen and also against the labelled antibody (acts as a procedure control). The buffer that is added removes the haemoglobin and helps visualise the coloured lines formed by the immobilised antigen-antibody complexes. The pLDH test detects a parasitemia of >100-200 parasites/µl. The pfHRP-2 detects >40 parasites/µl of asexual parasitemia [83].

The pfHRP-2 strips have 2 lines, 1 for the pfHRP-2 antigen and other for the control. The colour change in the control line is a must to validate the

test. If there is colour change in the test line without any colour change in the control line, the test is considered invalid.

In positive cases: colour change in both the control and test lines is interpreted as a positive test for Pfalciparum malaria as seen in fig 4.

In negative cases: colour changes only in the control line. There is no colour change in the test line.

Advantages of RDTs:

1. It is simple to perform. It doesn't require an equipment or trained technician.
2. **Sensitivity**: RDTs used in the diagnosis of P.falciparum have sensitivity >90% at parasite densities >100 parasites/µl of blood. But the sensitivity decreases when the density is < 100 parasites/µl. The sensitivity increases even more when the parasite density increases. In the diagnosis of P.vivax malaria, the pfHRP-2/PMA test has a less sensitivity compared to diagnosing P.falciparum malaria. But for the diagnosis of P.falciparum malaria, the pLDH test has a better sensitivity.
3. To diagnose malaria associated with pregnancy, HRP-2 appears to be a reliable marker.
4. pLDH is secreted only by the live parasites. So it can be used as a marker to monitor the treatment response. However, HRP-2 can remain positive for about 3-4 weeks even after completion of treatment [79].

5. The severity of the disease and parasitemia are directly proportional to the band intensity.

Disadvantages of RDTs:

1. RDT kits are expensive.
2. It cannot differentiate between the non-falciparum species.
3. False positive bands can appear. Some studies report that, RDTs cross react with autoantibodies like rheumatoid factor. The pfHRP-2 test and pLDH test appears to cross react but there appears no cross reactivity between PMA and rheumatoid factor.
4. Gametocytes cannot be detected.

QUANTITATIVE BUFFY COAT EXAMINATION (QBC):

An advanced technique discovered for malaria diagnosis is the QBC test for malaria.

QBC consists of three basic steps:

1. Concentrating the blood by centrifugation
2. Acridine orange staining
3. Examining under ultraviolet light source(fluorescence microscopy)

Principle: Acridine orange has the property to bind deoxyribonucleic acid and ribonucleic acids. The nucleus and cytoplasm of the malarial parasite binds Acridine orange [84]. When examined under fluorescent microscopy, they are

excited at 460nm (blue light) and the nucleus emits yellowish green fluorescence while the cytoplasm emits bright red fluorescence. The normal RBCs do not bind the stain because they are anucleated and so appear dark under the fluorescent light. In this dark background, the brightly fluorescent parasites are easily visualised. The general morphology of the parasite is well preserved.

Procedure:

- The currently available QBC capillary tube is internally precoated with Acridine orange stain.
- A sample of about 55-60 µl of blood is drawn in to the QBC tube by capillary action.
- A close fitting cylindrical float is inserted in to the capillary tube.
- Now the QBC tube is centrifuged at 12000 rpm for 5 minutes [85].
- The blood components separate based on their densities and form discrete bands.
- The interface between the RBC and WBC called the buffy coat region surrounding the float is examined using ultraviolet light under oil immersion.
- The entire circumference of the tube can be examined by rotating the QBC tube.
- The parasite can be visualised as bright fluorescent particles.

Results:

The following stages of parasites can be visualised.

- Crescent shaped gametocyte can be visualised in the lymphocyte platelet interface [86].
- Schizonts and mature trophozoites can appear in the granulocyte layer.
- Immature trophozoites that are ring shaped can appear throughout the red blood cell layer as shown in fig 5.

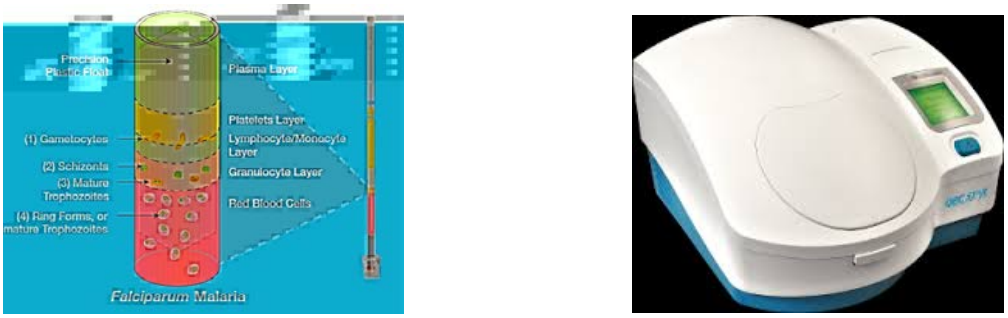

Fig 5 – QBC analyser and visualisation of parasite

Advantages of QBC:

1. QBC is more sensitive (as good as thick film)
2. QBC is faster.
3. Procedure doesn't require much trained technician.

Disadvantages of QBC: QBC is expensive and less specific.

Other less commonly used methods to diagnose malaria:

1. Antibody detection using test like ELISA that use soluble malarial antigen.

2. Culture techniques
3. Molecular diagnostic methods like PCR using PBRK 1 primer, which is 100 times more sensitive than thick smear.

Comparison of peripheral smear, QBC and RDT methods:

Feature	**Peripheral smear**	**QBC**	**RDT**
Method	Difficult	Easy	Easy
Time	Takes longer duration	Faster About 20-30 minutes	Faster About 15-30 minutes
Sensitivity	Detection limit: Thick film- 5 parasites/ul Thin film- 200 parasites/ul	Sensitive, as good as thick film	>90 % if parasite density >100 parasites/ul
Specificity	Gold standard	False positives can be reported	False positive due to cross reaction with rheumatoid factor
Specification	Thin film is gold standard	Difficult	Detects falciparum but non-falciparum species cannot be differentiated.

Cost	Cheap	Costly	Costly
Well trained microscopist	Required	Minimal training is enough	Minimal training is enough.

TREATMENT OF UNCOMPLICATED MALARIA CAUSED BY NON-FALCIPARUM SPECIES:

The second most causative agent of malaria in humans is P.vivax. About 35 % of the population in the world is at risk. About 9 % of the case of malaria worldwide is caused by P.vivax. P.vivax is prevalent in endemic areas in Asia, south and Central America and the Middle East.

Of all plasmodium species that affect human host, only P.ovale and P.vivax forms hypnozoites, that stay dormant in the liver and cause relapse. So, a single mosquito inoculation can result in multiple episode of illness.

Therefore, the main objective of treating infections caused by P.vivax and P.ovale is to cure both the blood and liver stage infections (radical cure), which prevents recrudescence and relapse respectively.

Susceptibility to antimalarial drugs: The susceptibility of P.vivax to antimalarials has been studied widely and studies support that P.vivax is still

much sensitive to chloroquine but there is an increasing resistance pattern. Only low level resistance has been found in parts of South east Asia and South America.

In areas with chloroquine sensitive P.vivax:

For vivax malaria, sensitive to chloroquine, oral chloroquine at a total dose of 25 mg (base)/kg body weight (BW) is well tolerated and effective [87].

Chloroquine is given at an initial dose of 10 mg/kg BW on day 1, followed by 10 mg/kg BW on day 2 and 5 mg/kg BW on day 3.

In areas with chloroquine resistant P.vivax:

Acts containing mefloquine, piperaquine or lumefantrine are the recommended treatment regimens.

Treatment of liver stages:

For the prevention of relapse, primaquine is given at a dose of 0.25 mg/kg BW daily for 14 days.

Primaquine is contraindicated in infants < 1 year of age, pregnant women and patients with G6PD deficiency. Primaquine can cause hemolysis in patients with G6PD deficiency. Therefore, primaquine should be administered with caution in areas with high prevalence of G6PD deficiency and should be tested if facilities are available.

Patients who develop symptoms like yellow conjunctiva, dark coloured urine, nausea, vomiting, abdominal pain and bluish discoloration of lips should be advised to stop primaquine and review to the physician.

TREATMENT OF P.FALCIPARUM MALARIA:

Artemisinin combination therapy (ACT) should be given to all cases of falciparum malaria confirmed by microscopy or RDT. This regimen should always be accompanied by primaquine single dose of 0.75 mg/kg BW on day 2.

ACT consists of an artemisinin derivative that is combined with long acting antimalarials like lumefantrine, amodiaquine, sulfadoxine-pyremethamine or mefloquine.

The National programme of India recommends ACT that contains artesunate 4 mg/kg BW daily for 3 consecutive days and one dose of sulfadoxine 25 mg/kg BW – pyrimethamine 1.25 mg/kg BW on day 0. Other ACT combinations like artesunate +amodiaquine, artmether+lumefantrine and artesunate+mefloquine can also be used [87, 88].

In uncomplicated malaria, artemisinin derivatives should never be used as monotherapy. These are rapidly acting drugs, when used alone, leads to development of drug resistance.

TREATMENT OF UNCOMPLICATED MALARIA IN PREGNANCY:

In uncomplicated vivax malaria, chloroquine can be used for treatment.

In uncomplicated falciparum malaria, quinine base 10 mg/kg/day for 7 days should be used in 1st trimester, while ACTs can be used for treatment in 2nd and 3rd trimesters.

General recommendations in the management of uncomplicated malaria [88]:

1. Starting treatment in empty stomach should be avoided. The first drug dose should be given under observation.
2. If vomiting occurs, dose should be repeated within 30 minutes.
3. If there is no improvement or if the situation deteriorates after 48 hours, patient should be advised to report back.
4. The patient should be examined for any other co-infections.

TREATMENT FAILURE/ DRUG RESISTANCE:

When the patient does not have parasitemia or fever till day 28, he is considered cured. When the patient does not respond, it may be due to treatment failure or drug resistance.

Early treatment failure (ETF):

- Development of severe malaria or danger signs on day 1, 2 or 3, with the presence of parasitemia [87].
- Increase in parasitemia on day 2 than on day 0, irrespective of axillary temperature.
- Presence of parasitemia on day 3 with axillary temperature>37.5 c.

- Parasitemia on day 3 with count > 25 % on day 0;

Late clinical failure (LCF):

- Development of severe malaria or danger signs in the presence of parasitemia on any day between day 4 and day 28 in those patients who did not previously fulfil any criteria of ETF [87].
- Presence of parasitemia on any day between day 4 and day 28 with axillary temperature > 37.5 c in those patients who did not previously fulfil any criteria of ETF.

Late parasitological failure (LPF):

- Presence of parasitemia on any day between day 7 and day 28 with axillary temperature that is < 37.5 c in patients who did not previously fulfil any criteria of ETF or LCF.
- These cases of falciparum malaria should be treated with alternative ACT or quinine with doxycycline. Doxycycline is contraindicated in children < 8 years old, pregnant and lactating women.

TREATMENT OF SEVERE MALARIA:

Studies show that untreated severe malaria approaches almost 100% mortality. The overall mortality rate falls to 10-20 % after effective antimalarial treatment. However, with the presence of associated complications, the risk of death increases. The risk mainly depends up on the species of malarial parasite,

the systems that are affected, the degree of organ dysfunction, immunity of the person, age, presence of concomitant illness and access to accurate treatment. The main objective in the treatment of severe malaria is preventing mortality [88].

Severe malaria is considered a medical emergency. In unconscious patients, airway should be secured and assessment of breathing and circulation should be done. After securing an intravenous access, blood glucose, haematocrit, parasitemia and renal functions should be measured. Lumbar puncture should be done in any unconscious patient for CSF analysis to rule out bacterial meningitis as a possible cause.

The presence of acidosis is an important determinant of outcome. The presence of sever acidosis is a poor prognostic factor. If available, plasma bicarbonate levels should be measured. Signs of meningeal irritation like neck stiffness, kernig's sign are usually not present in cerebral malaria, but opisthotonus may be present. There can be a clinical overlap between pneumonia, septicaemia and sever malaria. So in all cases, empirical broad spectrum parenteral antibiotics shoud be started along with antimalarial treatment.

Treatment regimen: Irrespective of chloroquine sensitivity, parenteral therapy should be used. Two classes of drug are available for parenteral treatment in severe malaria.

They are

1. Artemisinin derivatives
2. Cinchona alkaloids

Clinical trials show that there is substantial reduction in mortality with intravenous artesunate when compared to quinine and also artesunate is safe and sample to use.

So parenteral artesunate remains the treatment of choice in all severe malaria cases.

1. Artesunate:

Artesunate is available as powder of artesunic acid, and it is dissolved in 5% sodium bicarbonate to form sodium artesunate. This solution is then diluted with about 5 ml of 5 % dextrose and can be given as IM/IV injections [88].

The solution should not be stored and it should be freshly prepared for each administration. The main antimalarial effect is mediated by dihydroartemisinin, produced by rapid hydrolysis of artesunate.

Dosage and schedule:

Artesunate 2.4 mg/kg bw IV/IM given on the day of admission, then at 12 hours and 24 hours, following that once a day dose should be given.

2. **Quinine**:

Quinine was established for the treatment of severe malaria, in the early days itself. Various salts of quinine have been used parenterally, but dihydrochloride is the widely used drug.

Dosage and schedule:

Studies show that a loading dose of quinine, 20 mg salt/kg BW attains therapeutic concentrations within 4 hours. The maintenance dose of 10 mg salt/kg BW should be started 8 hours after the first dose, and should be administered every 8^{th} hourly. If patient requires parenteral quinine therapy for more than 48 hours, dose is reduced to 7 mg salt/kg BW 8^{th} hourly.

Caution:

- Quinine is dangerous when administered as rapid intravenous bolus dose, as it can result in lethal hypotension.
- Each dose of quinine should be diluted in 5% dextrose and infused over a period of 4 hours. It should be administered as a slow and rate controlled infusion with infusion rate not exceeding 5 mg salt/kg /hour.
- If controlled infusion is not possible, quinine can be given by IM injection in the anterior thigh. It should not be injected in the buttock to prevent injury to the sciatic nerve.
- Loading dose should not be given if the patient has already received quinine.

3. Artemether:

Artemether is less active than the active metabolite dihydroartemisinine. It can be given orally or as oil based intramuscular injection. IM artemether is absorbed slowly and erratically.

The initial dose of artemether is 3.2 mg/kg BW (IM in the anterior thigh). This is followed by a maintenance dose of 1.6 mg/kg BW IM daily.

Note:

- Once the patient is able to take orally, they should be switched to oral drugs.
- Patients who received parenteral quinine should be switched to oral quinine 10 mg/kg thrice a day to complete 7 days course, along with 3 mg/kg/day of doxycycline for 7 days. In cases where doxycycline is contraindicated, clindamycin 10 mg/kg BW 12th hourly for 7 days should be used.
- Patients, who received prenteral artemisinin derivatives, should complete full course of oral ACTs.
- Parenteral treatment should be given for a minimum period of 24 hours once started.

TREATMENT OF SEVERE MALARIA IN PREGNANCY:

In 1sttrimester, IV quinine should be used.

In 2nd and 3rd trimester of pregnancy, parenteral artemisinin derivatives can be given [87, 88].

Chemoprophylaxis:

Chemoprophylaxis is recommended for travellers, labourers and military persons exposed to infection in high endemic areas of malaria:

1. Short term chemoprophylaxis : (<6 weeks)
   - Doxycycline: 1.5mg/kg in children >8 years. The drug is started 2 days before and for 4 weeks after leaving the malaria endemic areas.

     It is contraindicated in pregnant, lactating woman and children <8 years.
   - Chloroquine: 5 mg/kg/week (max 300 mg base).It should be started 1 week before the travel.

2. Long term chemoprophylaxis: (>6 weeks)
   - Mefloquine: 5 mg/kg/week (max 250 mg).It should be administered 2 weeks before and 4 weeks after leaving the area. Mefloquine is contraindicated in patients with cardiac problem, history of seizures and neuropsychiatric problems.

MALARIA CONTROL STRATEGIES:

- **Early diagnosis and treatment:** This is the main strategy of malaria control. To prevent transmission, radical cure of malaria is necessary [87].

- **Vector control:**
    - **Chemical control:**
        - Indoor residual spray using insecticide can be used.
        - Aerosol space spray
        - Chemical larvicides can be used
        - During outbreaks, malathion fogging can be done.
    - **Biological control:**
        - Biocides can be used.
        - Biological larvicides like Gambusi aaffinis (fish) and Bacillus thuringiensis (bacteria) can be used to kill the mosquito larva.
    - **Personal protection:**
        - Wire mesh used for house screening.
        - Using insecticide treated bed nets
        - Using mosquito repellent creams, coils, liquids etc.
- **Environmental management and source reduction:**
    - Properly covering the stored water
    - Source reduction by filling the breeding places.
    - Channelization of breeding sources.

MATERIALS AND METHODS

STUDY CENTRE: Government R.S.R.M lying-in hospital, Stanley Medical College, Chennai.

STUDY DURATION: From January 2016 to August 2016

STUDY DESIGN: Cross Sectional study

STUDY POPULATION: All pregnant women who underwent delivery in Government R.S.R.M lying-in hospital during the study period.

SAMPLE SIZE: One hundred and ninety samples.

A Study population of 190 was selected based on the inclusion and exclusion criteria:

INCLUSION CRITERIA: All pregnant women who underwent delivery in Government R.S.R.M lying-in hospital during the study period, irrespective of the mode of delivery (Labour natural or Caesarean section) and the presence or absence of fever.

EXCLUSION CRITERIA: Those who did not give consent

METHODOLOGY:

The study was started after obtaining ethical clearance from the institutional ethical committee. All pregnant women who underwent delivery in

Government R.S.R.M lying-in hospital during the study period, irrespective of the mode of delivery and presence or absence of fever were enrolled. Informed written consent was obtained from all the patients. Those who refused to participate were excluded. History and details as per the proforma was filled. Blood samples were collected from the mother and placenta, for detection of malarial parasites by peripheral smear method and rapid diagnostic test (RDT). After initial stabilisation, the birth weight of the baby was recorded. Gestational age assessment was done based on last menstrual date and scored based on Modified Ballard scoring system. Peripheral blood sample was collected from the neonate, for detection of malarial parasites by peripheral smear method and RDT.

METHOD OF SAMPLE COLLECTION:

Maternal sample: Peripheral blood from mother was collected by finger prick method.

Placental sample:

After delivering the baby, placenta was removed. The placenta was then washed with 0.9 % normal saline. Then the placenta was kept with the fetal side (chorionic plate) facing down. This enhances the accumulation of blood and promotes accessibility of intervillous space.

Following this, a large bore needle attached to a syringe was inserted in to the intervillous space, that were denotes as dark-purple areas. Puncture of the surrounding fetal vessels were avoided. By gently pulling the syringe, a vacuum was created that initiated the blood flow into the syringe and the required amount of about 1 ml blood was withdrawn. The collected blood was used to perform rapid diagnostic test and both thick and thin smear were made for blood smear examination.

Neonatal sample:

Peripheral blood sample from the neonate was collected after initial stabilization. The blood was collected by heel prick method. The collected blood was used to do a smear study and RDT to detect malarial parasites.

From the samples collected, thick and thin smear were done and stained with Giemsa stain within 4 hours. The smears were then given specific codes and studied by a blinded pathologist and results interpreted. The diagnosis of malaria was based on the identification of asexual stages of plasmodium species on thick blood smear and species identified using thin blood smear. A minimum of 200 high power fields were examined for each thick and thin film before labelling a slide as negative for malarial parasite [90].

The collected samples were also used to perform Rapid diagnostic tests and results interpreted within 15-20 minutes. The RDT kit used were able to

identify specific infection by falciparum and by non-falciparum species. It couldn't differentiate between the non –falciparum species. Data obtained were entered in an excel sheet that was updated regularly. After completion of the study, the entered data was analysed using SPSS 16.0

Term definitions:

Gestational malaria: Parasite positivity in maternal peripheral blood.

Placental malaria: Parasite positivity in placental sample

Congenital malaria: Parasite positivity in neonatal peripheral blood at the time of birth (or) within first 7 days of life (or) cord blood parasite positivity [2].

Term neonate: Gestational age of completed 37 weeks.

Preterm neonate: Gestational age <37 weeks.

Postterm neonate: Gestational age >42 weeks

Normal birth weight: Birth weight ≥2.5kg.

Low birth weight: Birth weight <2.5kg.

Very low birth weight: Birth weight <1.5kg.

Maternal anemia: Haemoglobin level <11 gm/dl [89].

Severe maternal anemia: Haemoglobin level <7 gm/dl [89].

SAMPLE SIZE CALCULATION:

As this study is a cross sectional study the following formula was used for getting approximated sample size;

Sample size (n) = $(Z_\alpha)^2 * pq / d^2$

- Where Z_α is a standard value, for 5% type I error ($p<0.05$) the value is 1.96.
- p is the estimated prevalence rate. Prevalence rate of gestational malaria of 35% was taken for this study.
- q=100-p
- d (desired precision of prevalence) = 20 % of p

We calculated that 170 patients to be included in this study. As there was chance of refusal, we included 10% of the estimated population (n≈170+17) and included **190 participants** for this study.

STATISTICAL ANALYSIS:

Microsoft excel 2007 was used to tabulate and compute variables. SPSS version 16 (SPSS Inc, Chicago, 2007) was used for statistical analysis.

Results will be tabulated as 'mean ± SD' as appropriate. Students independent sample t test and Chi square test will be used to assess the

association between two variables. A p value of <0.05 will be considered as significant relationship between two variables.

The following tests will be applied for analysis:

Maternal age	Descriptive (as %)
Gravida	Descriptive (ratio or %)
Maternal haemoglobin levels	Descriptive (as %)
Placenta sample positivity (Yes / No)	Descriptive (ratio or %)
Positive results correlates with gravida (Yes / No)	Descriptive (as %) Correlation
Positive results correlates with maternal haemoglobin levels (Yes / No)	Descriptive (as %) Correlation
Positive results correlate with neonatal birth weight (Yes / No)	Descriptive (as %) Correlation
Positive results correlate with gestational age (yes/ No)	Descriptive (as %) Correlation

OBSERVATION AND RESULTS

The data collected from the study has been observed and analysed. The statistical significance was established as discussed in the following section:

AGE DISTRIBUTION

Of the 190 pregnant women included in the study, distribution based on age were analysed and the corresponding chart is shown as below.

AGE (in years)	FREQUENCY	PERCENTAGE
< 18	2	1.1
18-21	29	15.2
21-25	78	41.1
25-35	76	40
>35	5	2.6

Table 1 - Age distribution of pregnant women

Figure 6 represents that out 0f 190 pregnant women, 78 cases (41.1%) were in the age group 21-25 years which is the majority, followed by 76 cases (40%) between 25-35 years, 29 cases (15.2%) between 18-21 years, 5 cases (2.6%) above 35 years and the least of 2 cases (1.1%) less than 18 years.

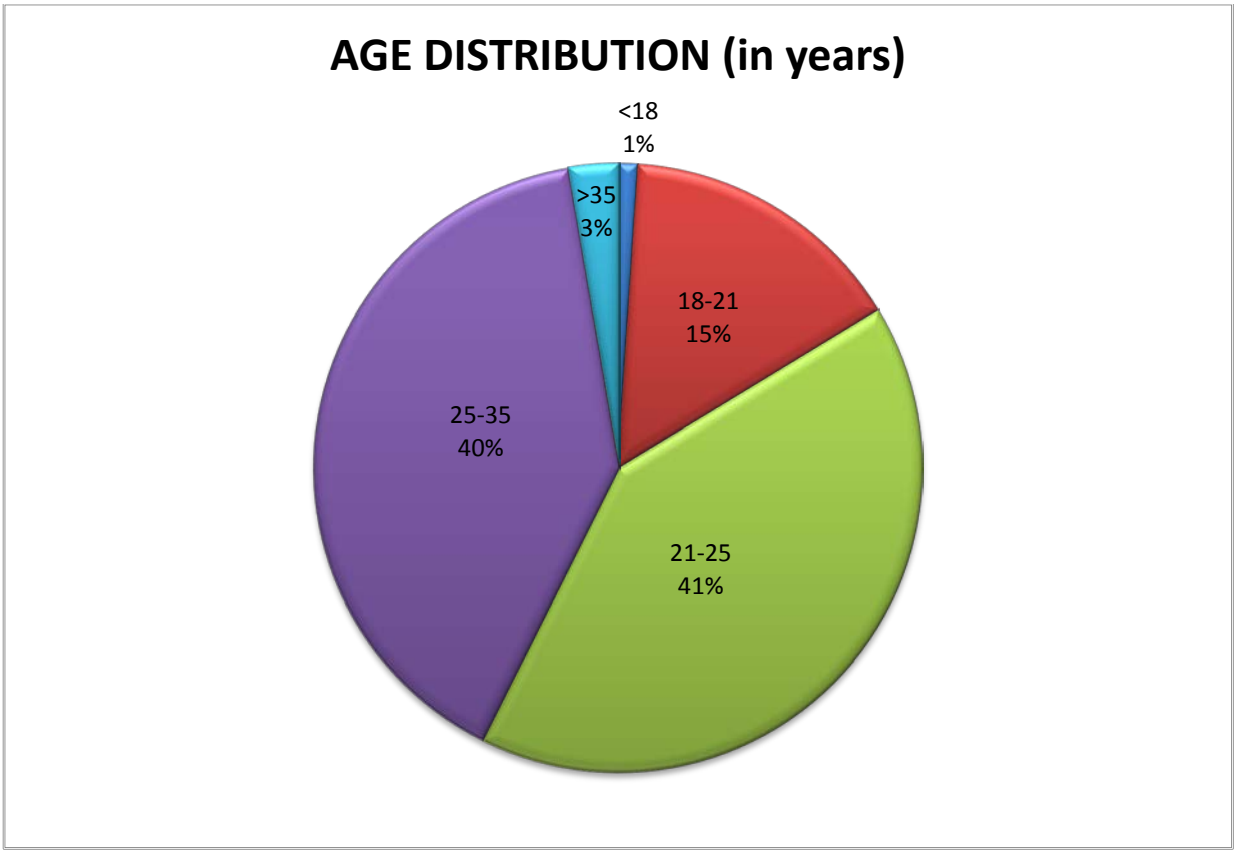

Fig 6 - Age distribution of pregnant women

DISTRIBUTION OF STUDY POPULATION BASED ON THE RESULTS OF PLACENTAL SAMPLE

	NO OF CASES
PLACENTAL PARASITEMIA POSITIVE	15(7.9%)
PLACENTAL PARASITEMIA NEGATIVE	175(92.1%)

Table 2 - Distribution of study population based on placental sample results

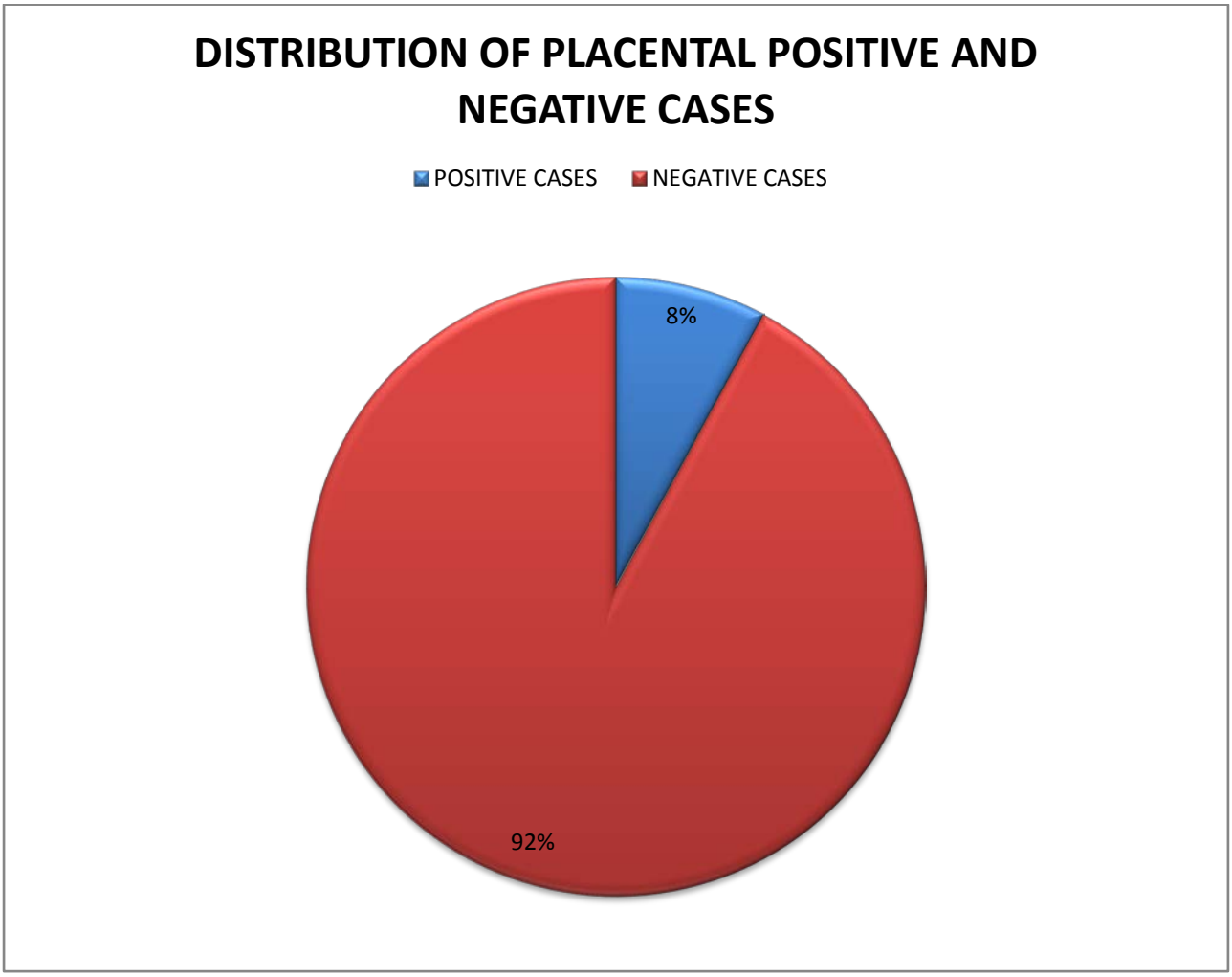

Fig 7 - Distribution of study population based on placental sample results

Among the 190 placental samples examined, 15 cases (7.9%) were positive for malarial parasite.

DISTRIBUTION OF STUDY POPULATION WITH PLACENTAL SAMPLE POSITIVE AND NEGATIVE CASES

Sample result	No of cases
Both placental RDT (PR) and smear (PP) negative	175
Only placental RDT positive	12
Only placental smear positive	1
Both placental RDT and smear positive	2

Table 3 - Distribution of placental samples positive and negative for malarial parasite.

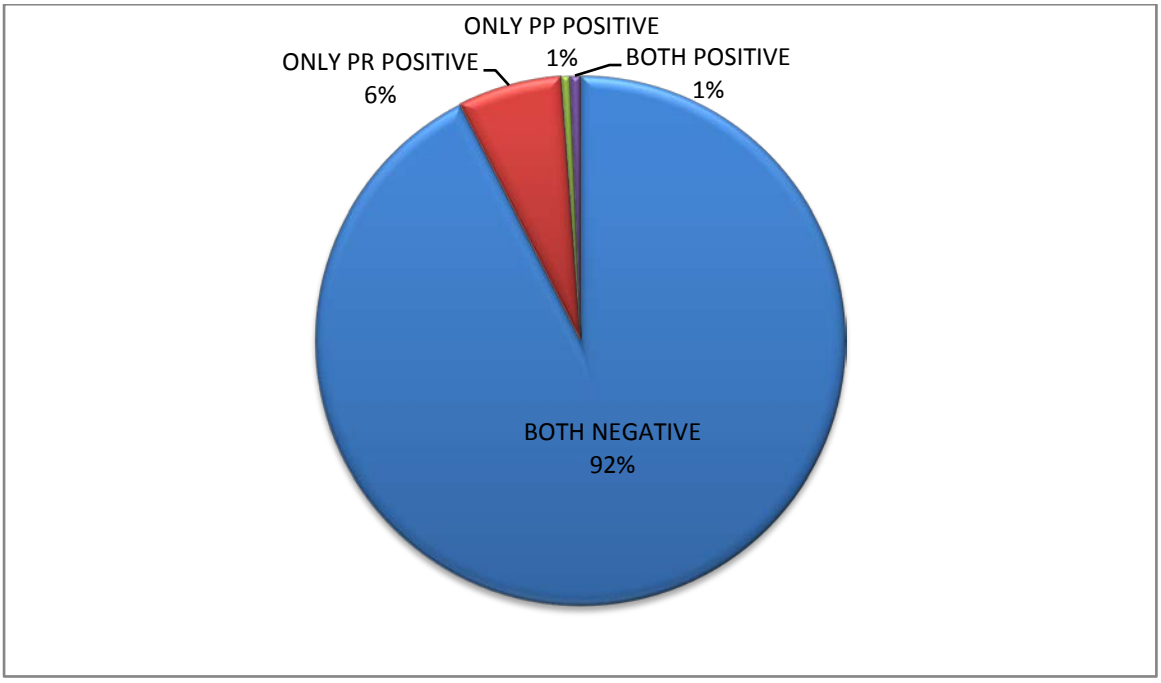

Fig 8 - Distribution of placental samples positive and negative for MP.

Among the 190 placental blood samples studies, 15 cases (7.9%) showed positivity. Of which 12 cases (6.3%) were positive only by placental RDT, 2 cases (1.1%) were positive by both placental RDT and smear study and 1 case (0.5%) was positive only by placental smear study.

DISTRIBUTION OF GRAVIDA AMONG POSITIVE AND NEGATIVE CASES

Gravidity	Total cases	Malaria positive Cases
1	92 (48.4%)	10 (5.3%)
2	59 (31%)	4 (2.1%)
3	24 (12.6%)	0
4	15 (7.9%)	1 (0.5%)

Table 4 - Distribution of gravid among positive and negative cases.

Among 190 pregnant women, 92 cases (48.4%) were primigravida which forms the majority, followed by 59 cases (31%) of gravida 2; 24 cases (12.6%) of gravida 3 and 15 cases (7.9%) of gravida 4.

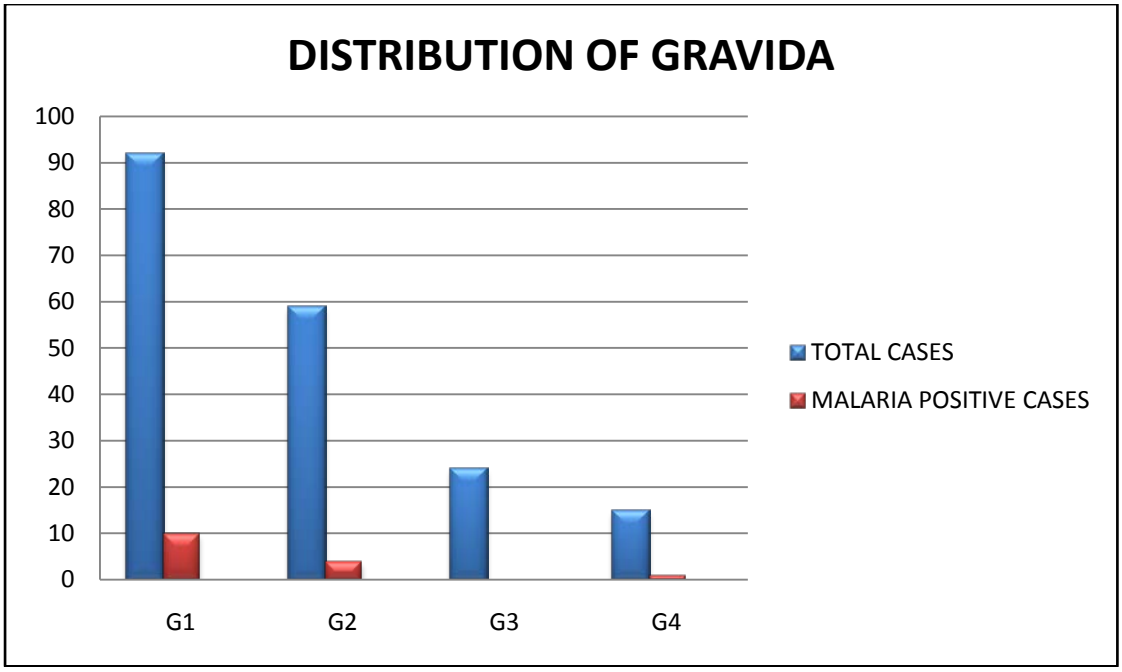

Fig 9 - Distribution of gravida among positive and negative cases.

DISTRIBUTION OF MATERNAL HAEMOGLOBIN LEVEL

	< 7 gm/dl	7-11 gm/dl	>11 gm/dl
Total cases	0	160	30
Positive cases	0	15	0

Table 5 - Distribution of maternal haemoglobin levels.

Fig 10 explains that among the 190 pregnant women, 160 cases (84%) presented with Hb levels < 11 gm/dl and only 30 cases (16%) were no anemic. Among the 15 placental positive cases, all had Hb values < 11 gm/dl and were anemic. None of the pregnant women in the study had severe anemia.

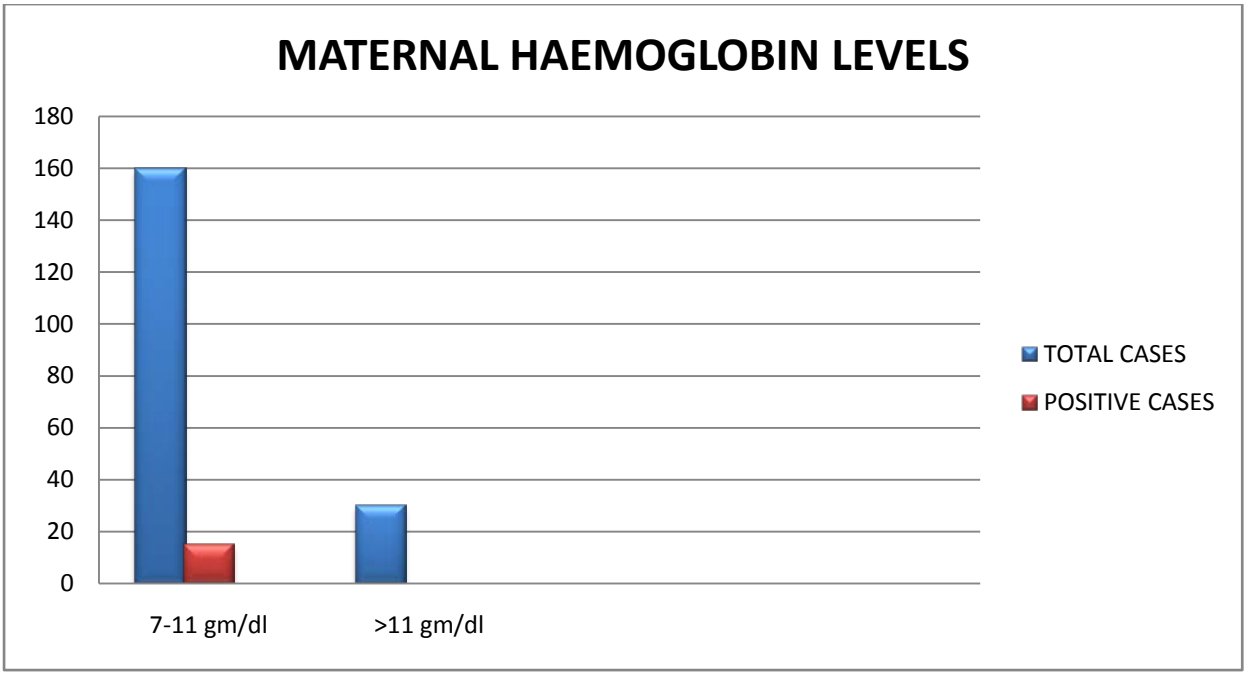

Fig 10 - Distribution of maternal haemoglobin levels.

DISTRIBUTION OF BIRTH WEIGHT AMONG POSITIVE AND NEGATIVE CASES

	≥2.5 kg	1.5- <2.5 kg	<1.5 kg
Positive cases	3 (1.6%)	11 (5.8%)	1 (0.5%)
Negative cases	116 (61.1%)	47 (24.7%)	12 (6.3%)

Table 6 - Distribution of birth weight

Out of the 175 neonates who were negative for placental malaria, 116 cases (61.1%) were ≥2.5 kg, followed by 47 cases (24.7%) between 1.5 to <2.5 kg and 12 cases (6.3%) less than 1.5 kg.

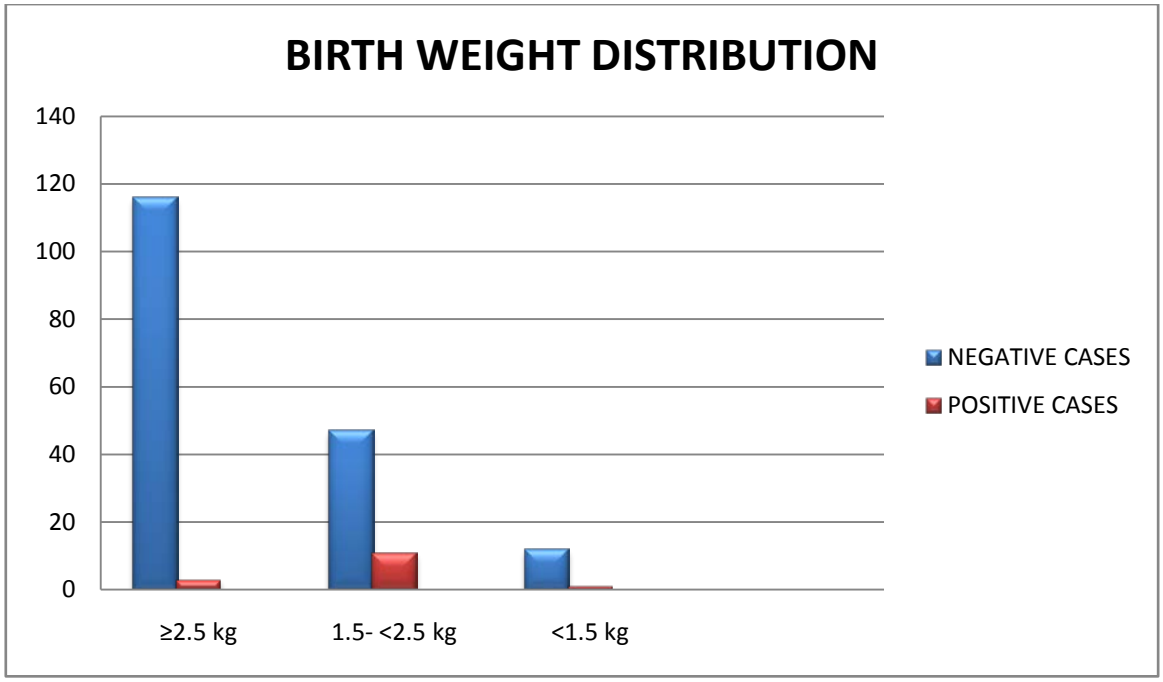

Fig 11 - Distribution of birth weight among positive and negative cases.

Among 15 cases positive for placental malaria, 11 cases (5.8%) were between 1.5 - <2.5 kg, followed by 3 cases (1.6%) more than 2.5 kg and 1 case (0.5%) less than 1.5 kg.

DISTRIBUTION OF GESTATIONAL AGE AMONG STUDY POPULATION

Total no of cases	190
Term babies	119 (63%)
Preterm babies	33 (17%)
Term SGA babies	38 (20%)

Table 7 - Distribution of gestational age among study population.

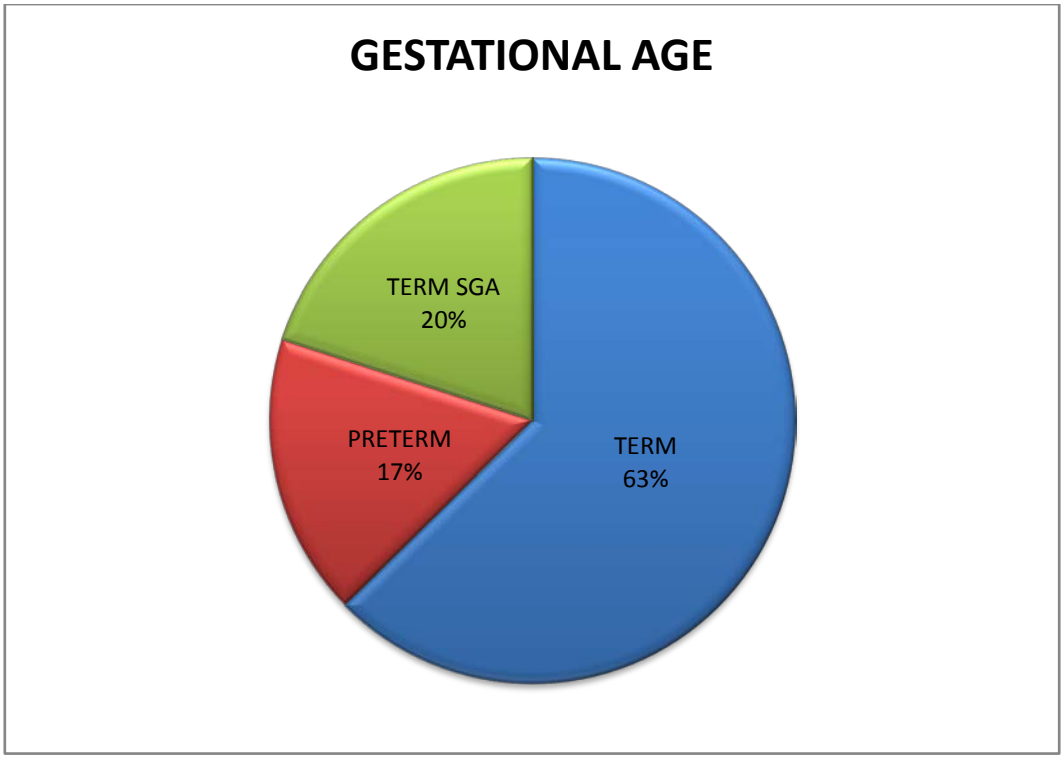

Fig 12 - Distribution of gestational age among study population.

Among 190 live births, 119 cases (63%) were term babies, followed by 38 (20%) term SGA babies and 33 (17%) preterm babies.

DISTRIBUTION OF GESTATIONAL AGE AMONG POSITIVE AND NEGATIVE CASES

	Term	Term SGA	Preterm
Placental RDT and smear negative cases	116	33	26
Placental RDT and smear positive cases	3	5	7

Table 8 - Distribution of Gestational age among positive and negative cases.

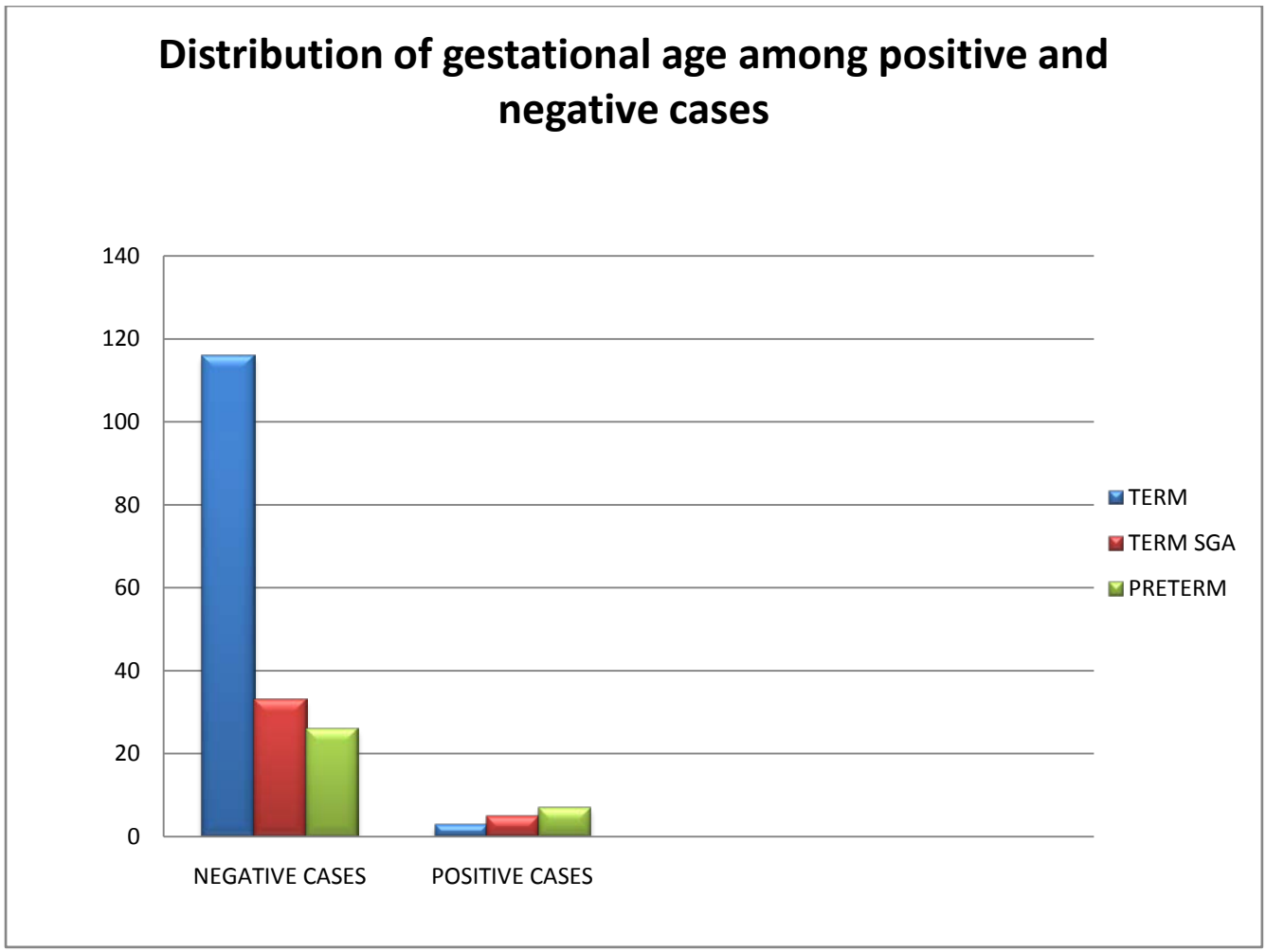

Fig 13 - Distribution of gestational age among positive and negative cases

Table 8 explains among the 15 positive cases, 7 cases (3.7%) were preterm followed by 5 (2.6%) term SGA babies and 3 (1.6%) term babies.

SIGNIFICANCE OF BIRTH WEIGHT, MATERNAL HEMOGLOBIN, AND GESTATIONAL AGE

BIRTH WEIGHT

NULL HYPOTHESIS	TEST	SIGNIFICANCE	DECISION
The distribution of mean birth weight is same among positive and negative cases	Student T test for 2 independent means t value is -2.96205	0.001725	Reject the null hypothesis

P value <0.05 is significant

From the above test it is inferred that the there is difference in mean birth weight among positive and negative cases.

MATERNAL HEMOGLOBIN:

NULL HYPOTHESIS	TEST	SIGNIFICANCE	DECISION
The distribution of maternal haemoglobin values is same among positive and negative cases	Student t test for 2 independent means t value is -3.03214	0.001386	Reject the null hypothesis

p value <0.05 is significant

From the above test it is inferred that there is difference in maternal haemoglobin values among positive and negative cases

GESTATIONAL AGE:

NULL HYPOTHESIS	TEST	SIGNIFICANCE	DECISION
The distribution of gestational age is same among malaria positive and negative cases	Chi-square test Pearson chi-square value is 14.222	0.000816	Reject the null hypothesis

$p < 0.05$ is significant

From the above test it is inferred that there is difference in gestational age among positive and negative cases.

DISCUSSION

In our study, a total of 200 pregnant women were enrolled. Of these 10 refused to participate and finally 190 were included in the study.

Of the 190 pregnant women included in our study, the mode of delivery was labour natural in 94 cases(49.5%), caesarean section in 95 cases(50%) and 1 case (0.5%) was delivered by emergency hysterotomy.

The pregnant women included in the study were aged between 17 and 39 years with a mean (SD) of 25.48 years (8.63). Among the pregnant women included, 92 cases (48.4%) were primigravida, 59 cases (31%) were gravida 2; 24 cases (12.6%) were gravida 3; 15 cases (7.9%) were gravida 4; none of them were above 4^{th} gravida.

The haemoglobin (Hb) levels of all the pregnant women ranged from 8.4 to 13.2g/dl, with a mean (SD) of 10.11 gm/dl (1.73). However, the total number of pregnant women with Hb level <11g/dl (criteria to define anemia by WHO) [89] was 160 cases (84%) and only 30 cases (16%) were not anemic. None of them had Hb levels <7g/dl. The Hb levels of all the 15 cases positive for placental parasitaemia was <11g/dl and were anemic.

Among the 190 samples taken from the pregnant mother, placenta and the neonate, none of the peripheral blood sample from the mother and the neonate showed positivity either by peripheral smear or by rapid diagnostic test.

A total of 15 cases (7.9%) showed placental malaria parasitemia. Among these 15 positive results, 12 samples (6.3%) were positive only by placental RDT, 2 samples (1.1%) were positive by both placental RDT and smear study and 1 sample (0.5%) was positive only by placental smear study. All the positive RDTs showed non-falciparum species, and all the positive smears showed Plasmodium vivax species. None of the smear/RDT showed positive for Plasmodium falciparum. Only few cases positive by smear study could be because of low parasite density in the placental sample.

These results were consistent with the study done by Olga Agudelo et al, in which 71 % of the study subjects had placenta malaria while only few cases were positive for malarial parasitemia in peripheral blood. This shows that absence of parasites in the mother's blood did not necessarily imply that the placenta was free of infection [90].

All the pregnant women delivered by either labour natural or caesarean section, resulted in live births. Of the 190 newborn, 119 cases (62.6%) were term babies, 38 cases (20%) were term SGA babies and 33 cases (17.4%) were preterm babies.

Among this distribution, that contributed by newborns born to placental parasitemia positive mothers were, 3 cases(1.6%) of term babies, 5 cases (2.6%) of term SGA babies and 7 cases (3.7%) of preterm babies. Preterm babies were higher among the positive cases.

PREVALENCE OF CONGENITAL MALARIA:

According to the study done by Innocent Chukwuemeka James Omalu et al [91] in Nigeria, there was less prevalence of congenital malaria. However, an increasing trend in prevalence of congenital malaria is being reported. In a multicentre study done at Ibadan, congenital malaria prevalence of 5.1% was reported [92]. A prevalence of 46% was reported in a sudy of 120 newborn babies at southwestern Nigeria [93]. A prevalence of 13% was reported among 546 in-born neonates at Calabar teaching hospital [94].

In a study conducted by Olga Agudelo et al [90] in Colombia, showed a low risk of congenital malaria, which strengthens the important role of passive transfer of maternal anti-malarial antibodies in the protection against congenital malaria.

According to study conducted by Juan G Pineros-Jimenez et al [95], among 116 newborns, 5 cases were found to be positive for parasitemia. Prevalence of congenital malaria was 4.3% according to this study.

In an Indian study done by Jyoti Singh et al [96] in Madhya Pradesh, of the 203 neonates studied, only 6 cases (3%) had parasitemia and concluded that despite a high prevalence of maternal smear positive malaria, the risk to the neonate is not high.

In our study, out of the 190 samples, none of the neonatal peripheral blood smear showed positivity. Several factors might explain the relative protection of the fetus from acquiring congenital malaria like the degree of previously acquired immunity of the mother, the proportion of fetal haemoglobin and the higher frequency of Plasmodium vivax infection which doesn't sequester much in the placenta.

GRAVIDITY IN RELATION TO MALARIA IN PREGNANCY:

According to the study conducted by Catherine O Falade et al [97] in Ibadan, among the 983 pregnant women included in the study, 366 women showed parasite positivity. Of the 366 positive results, 125 cases (34%) belonged to primigravida.

This was consistent with the done by Kailash Chandra Nayak et al [98] in India. In his study, of the 25 positive pregnant females, 18 belonged to primigravida when compared to other higher gravid.

According to a prospective study done by F Nosten et al [7], 47.5% of the study population belonged to primigravida, with a decrease in the number of affected women with increasing gravidity.

In contrast to this, a study conducted by Naseem Saba et al [99] in Pakisthan, 59.75% of the total 129 subjects included, belonged to multigravida.

Mc Gregor [100] and Hendrickse [101] proposed that the course of pregnancy related malaria might be different in areas of stable and unstable malaria. Supporting this, a study conducted by S.L.Sholapurkar et al [102] in Chandigarh which is an area of unstable malarial transmission, there was no correlation between parasite positivity and gravid, probably because of the absence of sufficient pre-existing immunity in both primigravida and multigravida.

In our study, among 15 positive cases, 10 cases (66.7%) were primigravida, which was higher than 4 cases (27%) by gravid 2 and 1 case (6.7%) by gravid 4. This result was consistent with most of the studies.

MATERNAL HAEMOGLOBIN LEVEL IN RELATION TO MALARIA:

Anemia as a complication in malaria infected person is known. And it is more severe in affected pregnant women.

In a study conducted by N.Singh et al [103] in Central India, there was a high prevalence of malaria in pregnant women. The study also showed that malarial infection was more frequent in primigravida and the infected pregnant women were significantly anemic than the non-infected pregnant women.

Similar results were provided by Nosten F et al [7] in his study, where 35.4% of the affected pregnant women were affected compared to 28.5% of the non-affected pregnant women, which was significant.

According to the study, conducted by Naseem saba et al [99], out of 129 pregnant women with malaria, 81 cases (62%) suffered from anemia and 48 cases (38%) had severe anemia, which was significant.

In our study, among 190 cases, 84 % (160 cases) were anemic and none of them suffered from severe anemia. This could be because almost 80% of the cases included were booked and were on regular antenatal follow up. All were provided with iron and folic acid tablets. They were routinely checked and treated for anemia in the antenatal clinics. However, a few had poor drug compliance. Out of 15 pregnant women positive for placental parasitemia, all were anemic with Hb level <11g/dl. But none of them showed Hb level <7g/dl.

BIRTH WEIGHT AND PLACENTAL MALARIA:

Regardless of the level of immunity, the main effects of malaria during pregnancy are maternal anemia and low birth weight of the newborn [104].

According to the study done by Menendez C et al [105] in Tanzania, there was a significant increase in the risk of low birth weight babies when the placenta was infected.

Similar study conducted by Catherine O Falade, Olukemi O et al [97], reported that low birth weight rate was higher among babies born to mothers with parasitemia than those without. The mean birth weight was found to be

lower in neonates of mother with peripheral and placental parasitemia by 138 g and 122 g respectively, which was statistically significant.

F.ter kuile et al [7] in their study reported a overall 123 g reduction in birth weight in newborns born to infected mother. These LBW babies were born to primigravida mothers. According to study done by Jyoti singh, Dharmendra soni et al [96], there was no significant association between low birth weight and maternal malarial infection. The results of this study are at variance with the data from other African studies.

Helen L.Guyatt et al [9] in their study, concluded that the risk of LBW associated with malarial infection was relatively consistent, with babies born to mothers with an infected placenta being twice as likely to be of LBW as those born to mothers with an uninfected placenta.

In our study, among the 15 positive cases 11 cases (73.3%) were between 1.5 - <2.5 kg, followed by 3 cases (20%) ≥2.5 kg and only 1 case (6.6%) less than 1.5 kg. The mean birth weight of the positive cases were 2175 gms which was 475 gms less than the mean birth weight (2650 gms) of negative cases and was statistically significant.

PREMATURITY AND PLACENTAL MALARIA:

C.Menendez et al [105] conducted a study, in which among 910 babies assessed for gestational age, 21% were preterm babies. And the proportion of

preterm babies was greater among primigravida than other parity groups. This study also described that, the massive monocyte infiltration of intervillous space by cytokines like IL-2, IFN-ɣ, IL-6 were associated with increased risk of prematurity.

According to the study conducted by, Christabel C Enweronu-Laryea et al [106], out of 405 newborns, 161(40%) were premature babies. These findings were consistent with studies done by Okoko BJ et al [107] and Mate Siakwa et al, which reported a significant association between placental malaria with preterm delivery and intrauterine growth retardation.

In our study, of all the 15 placental positive cases, 7 neonates (46.6%) were born preterm and 5 cases (33.3%) were term SGA babies, which was statistically significant.

CONCLUSION

The study conducted has enlightened on the following facts about congenital malaria and neonatal outcome in maternal malaria:

1. Among 190 placental samples examined, 15 cases (7.9%) were positive for malarial parasite, but none of them were symptomatic.
2. Among all peripheral blood samples from the mothers, none of them were positive either by peripheral smear or by RDT for malarial parasite.
3. There was no prevalence of congenital malaria in our area.
4. Placental malaria was more common in primigravida (66.7%) when compared to other gravidae.
5. The risk of low birth weight (80%) and prematurity (46.6%) were high in placental malaria, which was statistically significant (p value of 0.001725 and 0.000816 respectively).

LIMITATIONS OF THE STUDY:

1. Histopathological examination of placenta, which is a more reliable method of assessing placental infection was not done.
2. Sample size is relatively small.
3. Non-documentation of parasite density.

With the knowledge gained, steps should be taken to reduce pregnancy associated malaria.Important strategies to control malaria are effective case

management, use of insecticide treated nets (ITNs) and use of intermittent preventive therapy (IPTp).

The prevalence of malaria should be reduced overall to avoid exposure to the infection. Early case detection and prompt treatment is one of the main strategies of malaria control in India. Any pregnant women presenting with fever should be investigated for malaria and treated accordingly.

Indoor residual spraying (IRS) with residual insecticides is an effective vector control method. Effective use of IRS can be successful in reducing malaria in pregnancy burden because it can limit malaria transmission not only in the pregnant women, but also for the entire general population.

Pregnant women should be educated about the dangers and outcomes of malaria in pregnancy and awareness should be created. As a strategy to avoid exposure, widespread use of ITNs can be recommended. Great emphasis on providing ITNs to pregnant women is an important step towards alleviating malaria in pregnancy burden in our area.

In an area of stable malaria transmission like ours, most adult women have developed adequate level of immunity which results in asymptomatic infection and placental malaria. Placental malaria is most commonly associated with malaria-related anemia and low birth weight, due to presence of malarial parasite in the placenta. IPTp is an integral component of malaria in pregnancy

control in areas with stable transmission. Several studies in Africa have shown that IPTp with atleast 2 doses of sulphodoxine-pyrimethamine (SP) in the second and third trimesters of pregnancy significantly reduces the prevalence of maternal anemia, placental parasitemia and incidence of low birth weight. SP is considered safe for pregnant women with very limited side effects. However, the decision regarding use of IPTp in our area should be based on the results of studies conducted with large population and after knowing the resistance pattern of the region.

Prevention and control of malaria in pregnancy is an important and achievable goal. These strategies proposed can reduce the burden of malaria in pregnancy. It can effectively reduce the incidence of anemia in pregnant women, placental malaria and low birth weight babies.

What is already known?

Symptomatic cases of malaria in pregnancy can cause adverse neonatal outcome

What this study adds?

In areas with stable malarial transmission, even asymptomatic pregnant women who harbour parasite in the placenta (placental malaria) causes adverse neonatal outcome.

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PATIENT PROFORMA

PATIENT DETAILS:

- ✓ S.no
- ✓ Name
- ✓ Spouse name
- ✓ Age
- ✓ Residence

OBSTETRIC DETAILS:

- ✓ Obstetric score
- ✓ BOH
- ✓ HIV status
- ✓ Other infections
- ✓ Haemoglobin level
- ✓ Antenatal fever
- ✓ H/O Antimalarials
- ✓ If yes, name of the drug
- ✓ Pregnancy complications

BABY DETAILS:

- ✓ Birth weight
- ✓ Gestational age

  Preterm

  Term

  SGA

  Still birth

INVESTIGATIONS:

	PS study	RDT
Mothers blood		
Placental sample		
Newborn blood		

S.no	Name	Age in years	Gravida	Weight in kgs	Hb in gm/dl	HIV	Address	m.o.d	LMP	EDD	DOD
1	jeyashree	23	1	71	10.2	nr	new wpet	ln	10.7.15	17.4.16	7.4.16
2	thenmozhi	25	2	60	10.1	nr	madumanagar	ln	6.8.15	13.5.16	23.4.16
3	mahadevi	27	2	86	10.8	nr	kodungayur	ln	6.8.15	13.5.16	16.4.16
4	sudha	25	1	65	10.4	nr	thiruvottriyur	ln	29.12.15	5.10.16	11.9.16
5	bharathi	22	1	78	11.0	nr	kolathur	ln	28.11.15	5.9.16	7.9.16
6	janani	19	1	49	9.2	nr	kolathur	ln	7.12.15	14.9.16	11.9.16
7	amudha	30	2	44	10.8	nr	kargil nagar	ln	28.8.15	4.6.16	22.5.16
8	durga	20	1	65	10.3	nr	tondiarpet	ln	11.7.15	18.4.16	28.3.16
9	shahina begum	25	1	55	11.4	nr	tondiarpet	ln	28.8.15	4.6.16	28.5.16
10	gayathri	22	1	86	9.3	nr	kaladipet	ln	29.11.15	6.9.16	1.9.16
11	kavitha	34	4	72	11.4	nr	kodungayur	ln	9.12.15	16.9.16	9.9.16
12	abirami	26	2	63	11.5	nr	ponneri	ln	6.8.15	13.5.16	18.4.16
13	ravana	22	2	59	9.5	nr	nellore	ln	7.12.15	14.9.16	3.9.16
14	gayathri	25	2	64	9.8	nr	puzhal	ln	12.8.15	19.5.16	22.4.16
15	sumithra	29	2	44	10.3	nr	ennore	ln	24.7.15	31.4.16	24.4.16
16	vinothini	22	1	52	9.8	nr	ponneri	ln	20.1.15	27.10.16	4.9.16
17	swapna	24	1	68	10.4	nr	walltax road	ln	25.7.15	2.5.16	23.4.16
18	gowthami	30	2	58	9.8	nr	ponneri	lscs	27.7.15	3.5.16	22.4.16
19	christia	27	4	46	8.6	nr	old w.pet	ln	25.12.15	2.10.16	29.8.16
20	bommi	17	1	50	8.9	nr	korukupet	ln	nk	nk	22.4.16
21	rihana begum	25	4	70	12.6	nr	satri nagar	ln	7.12.15	14.9.16	11.9.16
22	lalitha	21	2	46	9.2	reactive	kaladipet	ln	12.8.16	19.5.16	22.4.16
23	vidhyalakshmi	23	2	50	9.0	nr	kaladipet	ln	15.1.16	22.10.16	24.8.16
24	yasmin	24	3	48	9.4	nr	old w.pet	ln	19.7..15	26.4.16	22.4.16
25	logeshwari	23	1	47	9.9	nr	ennore	ln	4.12.15	11.9.16	1.9.16
26	kalaiyarsi	20	1	50	9.6	nr	red hills	ln	19.7.15	26.4.16	22.4.16
27	sathya	30	2	47	9.2	nr	kumdipoondi	ln	10.8.15	17.5.16	22.4.16
28	kaveri	28	1	49	10.0	nr	kumidipoondi	ln	8.7.15	13.4.16	27.4.16
29	nandhini	22	3	50	8.4	nr	minjur	ln	2.1.16	9.10.16	10.9.16
30	saraswathi	30	3	55	9.4	nr	n.k.b. nagar	lscs	24.9.15	1.7.16	26.4.16
31	tamilselvi	21	1	68	10.5	nr	sastri nagar	ln	23.12.15	30.9.16	12.9.16
32	shynaz	22	1	60	9.4	nr	red hills	ln	27.7.15	3.5.16	22.4.16
33	muthulakshmi	23	2	74	10.7	nr	manali	ln	24.7.15	31.4.16	24.4.16
34	nirmala	35	3	75	11.8	nr	vyasarpadi	ln	19.7.15	26.4.16	22.4.16
35	tamilselvi	26	2	60	9.8	nr	kanjipuram	ln	19.7.15	26.4.16	20.4.16
36	syed ali	23	2	66	9.8	nr	vani nagar	ln	24.7.15	31.4.16	24.4.16
37	kushal banu	24	3	48	9.7	nr	patel nagar	ln	nk	nk	22.4.16
38	tamilselvi	28	2	52	10.0	nr	tondiarpet	ln	25.7.15	2.5.16	23.4.16
39	mithu	24	3	62	10.0	nr	butt road	ln	11.7.15	18.4.16	20.4.16
40	latha	30	4	70	10.8	nr	tondiarpet	ln	11.7.15	18.4.16	13.4.16
41	sindhu	19	1	60	10.0	nr	satri nagar	ln	11.7.15	18.4.16	17.4.16
42	krishnaveni	28	2	56	9.0	nr	sowcarpet	ln	10.7.15	17.4.16	20.4.16
43	anusia twin 1	38	1	63	9.4	nr	royapuram	lscs	28.8.15	4.6.16	20.4.16
44	anusia twin 2	38	1	63	9.4	nr	royapuram	lscs	28.8.15	4.6.16	20.4.16

45	nalini	28	4	60	11.4	nr	minjur	lscs	10.7.15	17.4.16	22.4.16
46	lakshmi	32	3	76	11.4	nr	minjur	lscs	10.7.15	17.4.16	22.4.16
47	bala	29	2	54	10.3	nr	kumidipoondi	lscs	19.7.15	26.4.16	22.4.16
48	sarawathi	24	3	63	10.3	nr	periyakuppam	lscs	13.7.15	20.4.16	21.4.16
49	uma raji	28	1	54	10.0	nr	tondiarpet	ln	10.8.15	17.5.16	22.4.16
50	dhanalakshmi	30	3	73	9.0	nr	ns garden	lscs	27.7.15	3.5.16	22.4.16
51	farhana	22	1	54	10.4	nr	dhesiya nagar	lscs	19.7.15	26.4.16	22.4.16
52	kalpana	29	2	64	9.0	nr	tondiarpet	hyste	28.10.15	4.8.16	23.4.16
53	gowri	25	2	74	10.3	nr	ponneri	ln	24.7.15	31.4.16	24.4.16
54	manjari	24	2	70	10.0	nr	jj nagar	lscs	nk	nk	27.4.16
55	usaina	21	1	50	9.8	nr	nethaji nagar	lscs	25.7.15	1.5.16	26.4.16
56	kanimozhi	24	3	69	10.7	nr	pudhupedu	lscs	26.7.15	2.5.16	26.4.16
57	yellamal	20	4	58	9.9	nr	kanchipuram	ln	nk	nk	24.4.16
58	banumathi	23	1	53	11.5	nr	aathur	ln	27.7.15	4.5.16	26.4.16
59	priya	23	1	43	9.4	nr	moolakothram	ln	26.7.15	2.5.16	26.4.16
60	chandra	33	3	72	11.0	nr	ponneri	ln	nk	nk	28.4.16
61	vidhya	21	1	60	9.7	nr	kumdipoondi	ln	27.1.16	4.11.16	27.8.16
62	rashmitha	24	1	45	10.2	nr	ponneri	ln	18.12.15	25.9.16	20.9.16
63	anjali	30	2	77	9.0	nr	thiruvallur	ln	20.7.15	27.4.16	27.4.16
64	suvitha	21	3	45	10.3	nr	ennore	ln	19.12.15	26.9.16	12.9.16
65	kowsar	23	1	54	9.8	nr	saidapet	lscs	2.12.15	9.9.16	9.9.16
66	nagammal	24	3	49	10.3	nr	korukupet	lscs	23.7.15	30.4.16	26.4.16
67	kaveri	25	1	52	10.1	nr	korukupet	lscs	23.7.15	30.4.16	23.4.16
68	girisha	23	1	60	10.4	nr	red hills	lscs	8.7.15	13.4.16	10.4.16
69	deepa	26	1	65	11.3	nr	sowcarpet	lscs	8.7.15	13.4.16	9.4.16
70	parvathy	27	2	50	9.8	nr	tondiarpet	lscs	23.7.15	30.4.16	1.5.16
71	nisha	22	1	50	10.3	nr	ponneri	lscs	25.12.15	2.9.16	6.9.16
72	manimegalai	23	2	73	9.2	nr	vyasarpadi	lscs	20.8.15	27.5.16	12.5.16
73	shubha	30	3	65	11.0	nr	ennore	ln	21.7.15	28.4.16	21.4.16
74	anitha	24	1	68	11.8	nr	vyasarpadi	lscs	nk	nk	11.5.16
75	sandhya	23	1	54	9.6	nr	kumdipoondi	lscs	9.7.15	14.4.16	9.4.16
76	revathi	30	2	60	10.8	nr	korukupet	ln	25.12.15	2.9.16	31.8.16
77	selvi	27	2	78	9.0	nr	kaladipet	lscs	23.7.15	30.4.16	5.4.16
78	srinisha	23	1	52	9.4	nr	kumdipoondi	ln	18.8.15	25.5.16	18.5.16
79	sairabanu	23	1	50	10.0	nr	old w .pet	lscs	21.7.15	28.4.16	20.4.16
80	devi	39	1	64	10.0	nr	royapuram	lscs	nk	nk	22.4.16
81	sandhya	28	2	52	10.5	nr	ezhil nagar	lscs	8.12.15	15.9.16	6.9.16
82	ammu	32	3	80	10.0	nr	tondiarpet	lscs	nk	nk	9.4.16
83	munni	26	1	65	10.6	nr	iynavaram	lscs	7.12.15	14.9.16	11.9.16
84	shakira	33	3	44	9.0	nr	ganeshpuram	lscs	20.8.15	27.5.16	22.5.16
85	archana	26	1	72	9.9	nr	vyasarpadi	lscs	5.12.15	12.9.16	12.9.16
86	kailam	23	2	66	9.8	nr	vani nagar	ln	24.7.15	31.4.16	24.4.16
87	keerthi	24	3	48	9.7	nr	patel nagar	ln	nk	nk	22.4.16
88	thamarai	28	2	52	10.0	nr	tondiarpet	ln	25.7.15	2.5.16	23.4.16
89	madhu	24	3	62	10.0	nr	butt road	ln	11.7.15	18.4.16	20.4.16

90	lavanya	30	4	70	10.8	nr	tondiarpet	ln	11.7.15	18.4.16	13.4.16
91	radha	30	1	64	9.2	nr	ponneri	lscs	6.8.15	13.5.16	18.4.16
92	sindhu	19	1	60	10.0	nr	satri nagar	ln	11.7.15	18.4.16	17.4.16
93	kavitha	28	2	56	9.0	nr	sowcarpet	ln	10.7.15	17.4.16	20.4.16
94	devi twin 1	38	1	63	9.4	nr	tondiarpet	lscs	28.8.15	4.6.16	20.4.16
95	devi twin 2	38	1	63	9.4	nr	tondiarpet	lscs	28.8.15	4.6.16	20.4.16
96	nalini	28	4	60	11.4	nr	minjur	lscs	10.7.15	17.4.16	22.4.16
97	logeshwari	32	3	76	11.4	nr	minjur	lscs	10.7.15	17.4.16	22.4.16
98	bavani	29	2	54	10.3	nr	kumidipoondi	lscs	19.7.15	26.4.16	22.4.16
99	sariga	24	3	63	10.3	nr	periyakuppam	lscs	13.7.15	20.4.16	21.4.16
100	usharani	28	1	54	10.0	nr	tondiarpet	ln	10.8.15	17.5.16	22.4.16
101	dhanam	30	3	73	9.0	nr	ns garden	lscs	27.7.15	3.5.16	22.4.16
102	fathima	22	1	54	10.4	nr	dhesiya nagar	lscs	19.7.15	26.4.16	22.4.16
103	salima	21	1	48	10.8	nr	old w.pet	lscs	12.8.15	19.5.16	22.4.16
104	lavanya	28	4	54	9.8	nr	sowcarpet	lscs	25.7.15	2..7.16	23.4.16
105	kavya	29	2	64	9.0	nr	tondiarpet	lscs	28.10.15	4.8.16	24.7.16
106	gomathi	25	2	74	10.3	nr	ponneri	ln	24.7.15	31.4.16	24.4.16
107	mumtaz	24	2	54	9.8	nr	kaladipet	lscs	nk	nk	12.9.16
108	kayalvizhi	34	2	62	9.2	nr	vyasarpadi	lscs	25.7.15	1.5.16	26.4.16
109	gowri	22	1	86	9.3	nr	kaladipet	ln	29.11.15	6.9.16	1.9.16
110	karpagam	34	2	63	11.4	nr	kodungayur	ln	9.12.15	16.9.16	9.9.16
111	anitha	26	2	63	11.5	nr	ponneri	ln	6.8.15	13.5.16	18.4.16
112	ragavi	22	2	59	9.5	nr	thiruvallur	ln	7.12.15	14.9.16	3.9.16
113	gayathri	25	2	64	9.8	nr	ponneri	ln	12.8.15	19.5.16	22.4.16
114	suseela	29	2	44	10.3	nr	ennore	ln	24.7.15	31.4.16	24.4.16
115	sargunam	24	1	68	10.4	nr	walltax road	ln	25.7.15	2.5.16	23.4.16
116	gowthami	30	2	58	9.8	nr	ponneri	lscs	27.7.15	4.5.16	22.4.16
117	chitra	27	1	46	8.6	nr	old w.pet	ln	25.12.15	2.10.16	29.8.16
118	boopali	17	1	50	8.9	nr	korukupet	ln	nk	nk	22.4.16
119	vanathi	21	2	55	9.6	nr	central	ln	nk	nk	23.4.16
120	rishika	25	4	70	12.6	nr	satri nagar	ln	7.12.15	14.9.16	11.9.16
121	lakshmi	21	2	46	10.2	nr	kaladipet	ln	12.8.16	19.5.16	22.4.16
122	vanitha	23	2	50	9.0	nr	kaladipet	ln	15.1.16	22.10.16	24.8.16
123	hemalatha	26	1	86	12.4	nr	royapuram	lscs	27.7.15	4.5.16	26.4.16
124	shobana	22	2	45	10.0	nr	ponneri	lscs	27.7.15	4.5.16	25.4.16
125	priyanka	27	1	56	10.0	nr	rajaji nagar	lscs	7.9.15	14.6.16	30.5.16
126	valarmathi	28	2	55	9.5	nr	kadhi street	lscs	19.7.15	26.4.16	22.4.16
127	gandhimathi	29	4	48	12.0	nr	ponneri	lscs	27.7.15	3.5.16	22.4.16
128	indhumathy	25	1	66	9.8	nr	minjur	ln	10.7.15	17.4.16	18.4.16
129	kokila	26	1	53	10.2	nr	old w.pet	lscs	13.7.15	20.4.16	18.4.16
130	komala	28	1	65	12.0	nr	maadhavaram	lscs	26.7.15	3.5.16	27.4.16
131	suganya	26	1	60	10.6	nr	old w.pet	lscs	1.12.16	8.9.16	6.9.16
132	rekha	19	1	50	9.4	nr	tondiarpet	lscs	7.9.15	14.6.16	26.4.16
133	vinitha	19	1	52	10.3	nr	ponneri	lscs	27.7.15	4.5.16	26.4.16
134	absha	21	1	50	9.7	nr	thiruvottriyur	ln	24.9.15	1.7.16	26.4.16

135	haseena	22	4	54	9.6	nr	madhavaram	lscs	10.9.15	17.6.16	27.5.16
136	nirmala	20	1	60	11.4	nr	edapalayam	lscs	8.7.15	13.4.16	27.4.16
137	anithamary	30	2	74	9.6	nr	ponneri	lscs	20.7.15	27.4.16	27.4.16
138	ramulamma	20	1	54	9.8	nr	thiruvottriyur	ln	23.7.15	30.4.16	1.5.16
139	nagavalli	22	1	60	9.0	nr	kosapoor	ln	23.8.15	30.5.16	2.5.16
140	mangayarkani	29	1	71	10.3	nr	pavalakulam	lscs	30.8.15	6.6.16	2.5.16
141	aruna	23	1	56	10.2	nr	tondiarpet	lscs	28.8.15	4.6.16	5.5.16
142	priya	22	1	60	10.0	nr	sathyanagar	lscs	14.8.15	21.5.16	5.5.16
143	thenmozhi	20	1	54	11.0	nr	minjur	lscs	31.7.15	7.5.16	6.5.26
144	rizwana begum	27	3	60	10.6	nr	kaladipet	ln	2.8.15	9.5.16	6.5.16
145	ramaprabha	23	1	56	11.0	nr	w.pet	lscs	4.8.15	11.5.16	6.5.16
146	padma	26	2	56	12.2	nr	kondi thopu	lscs	17.8.15	24.5.16	6.5.16
147	rehana begam	29	4	65	11.0	nr	perambur	lscs	3.8.15	10.5.16	12.5.16
148	rekha	25	1	54	10.2	nr	vyasarpadi	lscs	16.8.15	23.5.16	12.5.16
149	suganya	23	1	56	13.2	nr	gandhi puram	lscs	20.8.15	27.5.16	12.5.16
150	manju	24	2	58	10.0	nr	ponneri	lscs	27.8.15	3.6.16	12.5.16
151	malathi	20	2	44	9.6	nr	ponneri	lscs	19.8.15	26.5.16	12.5.16
152	rajeshwari	24	1	57	10.8	nr	korukupet	lscs	18.8.15	25.5.16	12.5.16
153	surya	20	1	46	10.5	nr	tondiarpet	ln	11.8.15	18.5.16	12.5.16
154	priya	24	1	66	9.9	nr	veechur	ln	19.8.15	26.5.16	9.5.16
155	sasikala	25	1	60	9.0	nr	kanchipuram	ln	22.8.15	29.5.16	29.5.16
156	selvi	20	1	56	10.0	nr	ponneri	ln	1.9.15	8.6.16	28.5.16
157	priya	24	3	74	9.8	nr	ponneri	ln	nk	nk	25.5.16
158	gangadevi	28	2	68	10.2	nr	sastri nagar	ln	31.7.15	7.5.16	25.5.16
159	vijayalakshmi	25	2	54	10.0	nr	tondiarpet	lscs	18.9.15	25.6.16	28.5.16
160	rajabnisha	30	4	78	9.4	nr	korukupet	lscs	18.9.15	25.6.16	28.5.16
161	suganya	23	1	60	12.0	nr	kanchipuram	lscs	19.8.15	26.5.16	28.5.16
162	jayachitra	21	1	56	9.8	nr	kaladipet	ln	3.10.15	10.7.16	28.5.16
163	uma	23	2	74	9.9	nr	karapettai	lscs	14.8.15	21.5.16	28.5.16
164	indhumathy	23	2	75	9.7	nr	thiruvallur	lscs	5.9.15	12.6.16	27.5.16
165	malliga	28	1	58	10.5	nr	kanji nagar	lscs	4.9.15	11.6.16	27.5.16
166	priya	21	1	59	9.9	nr	royapuram	lscs	20.8.15	27.5.16	27.5.16
167	ponmalar	30	1	62	10.0	nr	kodungayur	ln	5.9.15	12.6.16	27.5.16
168	preethi	29	1	75	10.6	nr	ennore	lscs	16.9.15	23.6.16	27.5.16
169	vinitha	21	1	60	12.0	nr	anna nagar	lscs	23.8.15	30.5.16	27.5.16
170	kokilakshmi	24	2	80	10.2	nr	jj nagar	ln	20.8.15	27.5.16	27.5.16
171	maheshwari	29	1	65	10.2	nr	tondiarpet	lscs	24.8.15	1.6.16	27.5.16
172	sivaranjani	23	1	60	10.0	nr	kodungayur	lscs	20.8.15	27.5.16	24.5.16
173	divya	23	1	66	10.0	nr	solavaram	lscs	31.8.15	7.6.16	24.5.16
174	arokayamary	35	2	61	9.3	nr	puzhal	lscs	13.8.15	20.5.16	24.5.16
175	susila	26	2	61	12.0	nr	palli karanai	lscs	15.8.15	22.5.16	20.5.16
176	uma	34	3	82	10.4	nr	mannadi	lscs	nk	nk	23.5.16
177	velankani	19	1	42	9.0	nr	ponneri	lscs	11.7.15	18.4.16	28.3.16
178	vaidhegi	21	2	55	9.6	nr	central	ln	nk	nk	23.4.16
179	lavanya	27	1	46	8.6	nr	korukupet	ln	10.7.15	17.4.16	3.4.16

180	rahamth	30	1	64	9.2	nr	ponneri	lscs	6.8.15	13.5.16	18.4.16
181	soundarya	21	1	48	9.8	nr	old w.pet	lscs	12.8.15	19.5.16	22.4.16
182	lakshmi	28	4	54	9.8	nr	sowcarpet	lscs	25.7.15	2.7.16	23.4.16
183	indhra	26	1	82	10.8	nr	tondiarpet	ln	10.2.16	17.11.16	28.8.16
184	susila	22	1	46	9.0	nr	tondiarpet	lscs	10.9.15	17.6.16	27.4.16
185	tamilselvi	25	1	69	9.9	nr	ponneri	ln	21.7.15	28.4.16	22.4.16
186	rajeshwari	24	1	60	9.5	nr	korukupet	lscs	25.7.15	1.5.16	26.4.16
187	prema	22	1	45	9.2	nr	thiruvottriyur	lscs	20.8.15	27.5.16	3.5.16
188	varalakshmi	22	1	52	9.8	nr	ponneri	ln	20.1.15	27.10.16	4.9.16
189	praveena	22	2	54	9.9	nr	ennore	lscs	26.7.25	2.5.16	26.4.16
190	jini	30	2	67	9.0	nr	sharma nagar	lscs	14.8.15	21.5.16	14.5.16

S.no	Name	Age in years	BW in kg	GA	MR	MP	PR	PP	BR	BP
1	jeyashree	23	2.195	term sga	neg	neg	neg	neg	neg	neg
2	thenmozhi	25	2.490	term sga	neg	neg	neg	neg	neg	neg
3	mahadevi	27	2.700	term	neg	neg	neg	neg	neg	neg
4	sudha	25	2.730	term	neg	neg	neg	neg	neg	neg
5	bharathi	22	3.180	term	neg	neg	neg	neg	neg	neg
6	janani	19	2.590	term	neg	neg	neg	neg	neg	neg
7	amudha	30	2.530	term	neg	neg	neg	neg	neg	neg
8	durga	20	2.495	term sga	neg	neg	neg	neg	neg	neg
9	shahina begum	25	2.730	term	neg	neg	neg	neg	neg	neg
10	gayathri	22	3.830	term	neg	neg	neg	neg	neg	neg
11	kavitha	34	2.695	term	neg	neg	neg	neg	neg	neg
12	abirami	26	2.000	term sga	neg	neg	neg	neg	neg	neg
13	ravana	22	2.510	term	neg	neg	neg	neg	neg	neg
14	gayathri	25	2.950	term	neg	neg	neg	neg	neg	neg
15	sumithra	29	2.315	term sga	neg	neg	neg	neg	neg	neg
16	vinothini	22	1.645	preterm	neg	neg	neg	neg	neg	neg
17	swapna	24	3.530	term	neg	neg	neg	neg	neg	neg
18	gowthami	30	3.004	term	neg	neg	neg	neg	neg	neg
19	christia	27	1.625	preterm	neg	neg	neg	neg	neg	neg
20	bommi	17	2.790	term	neg	neg	neg	neg	neg	neg
21	rihana begum	25	3.365	term	neg	neg	neg	neg	neg	neg
22	lalitha	21	2.020	preterm	neg	neg	neg	neg	neg	neg
23	vidhyalakshmi	23	1.484	preterm	neg	neg	neg	neg	neg	neg
24	yasmin	24	2.145	term sga	neg	neg	neg	neg	neg	neg
25	logeshwari	23	2.480	term sga	neg	neg	neg	neg	neg	neg
26	kalaiyarsi	20	2.535	term	neg	neg	neg	neg	neg	neg
27	sathya	30	1.900	preterm	neg	neg	neg	neg	neg	neg
28	kaveri	28	2.230	term sga	neg	neg	neg	neg	neg	neg
29	nandhini	22	1.425	preterm	neg	neg	neg	neg	neg	neg
30	saraswathi	30	1.450	preterm	neg	neg	neg	neg	neg	neg
31	tamilselvi	21	1.260	term	neg	neg	neg	neg	neg	neg
32	shynaz	22	3.040	term	neg	neg	neg	neg	neg	neg
33	muthulakshmi	23	3.200	term	neg	neg	neg	neg	neg	neg
34	nirmala	35	2.950	term	neg	neg	neg	neg	neg	neg
35	tamilselvi	26	2.695	term	neg	neg	neg	neg	neg	neg
36	syed ali	23	2.470	term sga	neg	neg	neg	neg	neg	neg
37	kushal banu	24	2.010	preterm	neg	neg	neg	neg	neg	neg
38	tamilselvi	28	2.935	term	neg	neg	neg	neg	neg	neg
39	mithu	24	3.850	term	neg	neg	neg	neg	neg	neg
40	latha	30	2.555	term	neg	neg	neg	neg	neg	neg
41	sindhu	19	2.510	term	neg	neg	neg	neg	neg	neg
42	krishnaveni	28	2.265	term sga	neg	neg	neg	neg	neg	neg
43	anusia twin 1	38	1.240	preterm	neg	neg	neg	neg	neg	neg
44	anusia twin 2	38	1.405	preterm	neg	neg	neg	neg	neg	neg
45	nalini	28	3.550	term	neg	neg	neg	neg	neg	neg
46	lakshmi	32	2.325	term sga	neg	neg	neg	neg	neg	neg
47	bala	29	2.820	term	neg	neg	neg	neg	neg	neg
48	sarawathi	24	2.815	term	neg	neg	neg	neg	neg	neg
49	uma raji	28	1.900	term sga	neg	neg	neg	neg	neg	neg
50	dhanalakshmi	30	3.020	term	neg	neg	neg	neg	neg	neg
51	farhana	22	2.950	term	neg	neg	neg	neg	neg	neg

52	kalpana	29	4.900	preterm	neg	neg	neg	neg	neg	neg
53	gowri	25	2.315	term sga	neg	neg	neg	neg	neg	neg
54	manjari	24	2.735	term	neg	neg	neg	neg	neg	neg
55	usaina	21	2.695	term	neg	neg	neg	neg	neg	neg
56	kanimozhi	24	3.415	term	neg	neg	neg	neg	neg	neg
57	yellamal	20	2.900	term	neg	neg	neg	neg	neg	neg
58	banumathi	23	2.860	term	neg	neg	neg	neg	neg	neg
59	priya	23	3.300	term	neg	neg	neg	neg	neg	neg
60	chandra	33	3.220	term	neg	neg	neg	neg	neg	neg
61	vidhya	21	1.480	preterm	neg	neg	neg	neg	neg	neg
62	rashmitha	24	2.950	term	neg	neg	neg	neg	neg	neg
63	anjali	30	3.630	term	neg	neg	neg	neg	neg	neg
64	suvitha	21	2.745	term	neg	neg	neg	neg	neg	neg
65	kowsar	23	2.840	term	neg	neg	neg	neg	neg	neg
66	nagammal	24	3.355	term	neg	neg	neg	neg	neg	neg
67	kaveri	25	2.600	term	neg	neg	neg	neg	neg	neg
68	girisha	23	2.340	term sga	neg	neg	neg	neg	neg	neg
69	deepa	26	3.250	term	neg	neg	neg	neg	neg	neg
70	parvathy	27	2.760	term	neg	neg	neg	neg	neg	neg
71	nisha	22	2.560	term	neg	neg	neg	neg	neg	neg
72	manimegalai	23	3.260	term	neg	neg	neg	neg	neg	neg
73	shubha	30	2.460	term sga	neg	neg	neg	neg	neg	neg
74	anitha	24	2.210	term sga	neg	neg	neg	neg	neg	neg
75	sandhya	23	2.905	term	neg	neg	neg	neg	neg	neg
76	revathi	30	2.720	term	neg	neg	neg	neg	neg	neg
77	selvi	27	2.020	preterm	neg	neg	neg	pos	neg	neg
78	srinisha	23	3.005	term	neg	neg	neg	neg	neg	neg
79	sairabanu	23	2.465	term sga	neg	neg	neg	neg	neg	neg
80	devi	39	1.230	preterm	neg	neg	neg	neg	neg	neg
81	sandhya	28	2.910	term	neg	neg	neg	neg	neg	neg
82	ammu	32	3.040	term	neg	neg	neg	neg	neg	neg
83	munni	26	2.840	term	neg	neg	neg	neg	neg	neg
84	shakira	33	2.950	term	neg	neg	neg	neg	neg	neg
85	archana	26	2.890	term	neg	neg	neg	neg	neg	neg
86	kailam	23	2.470	term sga	neg	neg	neg	neg	neg	neg
87	keerthi	24	2.010	term sga	neg	neg	neg	neg	neg	neg
88	thamarai	28	2.935	term	neg	neg	neg	neg	neg	neg
89	madhu	24	3.850	term	neg	neg	neg	neg	neg	neg
90	lavanya	30	2.555	term	neg	neg	neg	neg	neg	neg
91	radha	30	2.000	preterm	neg	neg	neg	neg	neg	neg
92	sindhu	19	2.510	term	neg	neg	neg	neg	neg	neg
93	kavitha	28	2.265	term sga	neg	neg	neg	neg	neg	neg
94	devi twin 1	38	1.340	preterm	neg	neg	neg	neg	neg	neg
95	devi twin 2	38	1.230	preterm	neg	neg	neg	neg	neg	neg
96	nalini	28	3.550	term	neg	neg	neg	neg	neg	neg
97	logeshwari	32	2.325	term sga	neg	neg	neg	neg	neg	neg
98	bavani	29	2.820	term	neg	neg	neg	neg	neg	neg
99	sariga	24	2.815	term	neg	neg	neg	neg	neg	neg
100	usharani	28	1.900	term sga	neg	neg	neg	neg	neg	neg
101	dhanam	30	3.020	term	neg	neg	neg	neg	neg	neg
102	fathima	22	2.950	term	neg	neg	neg	neg	neg	neg
103	salima	21	2.140	preterm	neg	neg	neg	neg	neg	neg

104	lavanya	28	3.580	term	neg	neg	neg	neg	neg	neg
105	kavya	29	2.530	term	neg	neg	neg	neg	neg	neg
106	gomathi	25	2.315	term sga	neg	neg	neg	neg	neg	neg
107	mumtaz	24	2.145	term sga	neg	neg	neg	neg	neg	neg
108	kayalvizhi	34	2.620	term	neg	neg	neg	neg	neg	neg
109	gowri	22	3.830	term	neg	neg	neg	neg	neg	neg
110	karpagam	34	2.695	term	neg	neg	neg	neg	neg	neg
111	anitha	26	2.000	term sga	neg	neg	neg	neg	neg	neg
112	ragavi	22	2.510	term	neg	neg	neg	neg	neg	neg
113	gayathri	25	2.850	term	neg	neg	neg	neg	neg	neg
114	suseela	29	2.315	term sga	neg	neg	neg	neg	neg	neg
115	sargunam	24	3.530	term	neg	neg	neg	neg	neg	neg
116	gowthami	30	3.004	term	neg	neg	neg	neg	neg	neg
117	chitra	27	1.725	preterm	neg	neg	neg	neg	neg	neg
118	boopali	17	2.800	term	neg	neg	neg	neg	neg	neg
119	vanathi	21	2.065	term sga	neg	neg	neg	neg	neg	neg
120	rishika	25	3.465	term	neg	neg	neg	neg	neg	neg
121	lakshmi	21	2.020	preterm	neg	neg	neg	neg	neg	neg
122	vanitha	23	1.484	preterm	neg	neg	neg	neg	neg	neg
123	hemalatha	26	2.960	term	neg	neg	neg	neg	neg	neg
124	shobana	22	2.660	term	neg	neg	neg	neg	neg	neg
125	priyanka	27	3.430	term	neg	neg	neg	neg	neg	neg
126	valarmathi	28	3.280	term	neg	neg	neg	neg	neg	neg
127	gandhimathi	29	2.905	term	neg	neg	neg	neg	neg	neg
128	indhumathy	25	3.600	term	neg	neg	neg	neg	neg	neg
129	kokila	26	3.175	term	neg	neg	neg	neg	neg	neg
130	komala	28	2.580	term	neg	neg	neg	neg	neg	neg
131	suganya	26	2.715	term	neg	neg	neg	neg	neg	neg
132	rekha	19	1.675	preterm	neg	neg	neg	neg	neg	neg
133	vinitha	19	3.085	term	neg	neg	neg	neg	neg	neg
134	absha	21	1.440	preterm	neg	neg	neg	neg	neg	neg
135	haseena	22	2.140	preterm	neg	neg	neg	neg	neg	neg
136	nirmala	20	2.240	term sga	neg	neg	neg	neg	neg	neg
137	anithamary	30	3.635	term	neg	neg	neg	neg	neg	neg
138	ramulamma	20	2.590	term	neg	neg	neg	neg	neg	neg
139	nagavalli	22	2.655	term	neg	neg	neg	neg	neg	neg
140	mangayarkani	29	2.080	preterm	neg	neg	neg	neg	neg	neg
141	aruna	23	1.870	preterm	neg	neg	neg	neg	neg	neg
142	priya	22	2.710	term	neg	neg	neg	neg	neg	neg
143	thenmozhi	20	2.600	term	neg	neg	neg	neg	neg	neg
144	rizwana begum	27	2.340	term sga	neg	neg	neg	neg	neg	neg
145	ramaprabha	23	3.660	term	neg	neg	neg	neg	neg	neg
146	padma	26	2.600	term	neg	neg	neg	neg	neg	neg
147	rehana begam	29	2.695	term	neg	neg	neg	neg	neg	neg
148	rekha	25	2.650	term	neg	neg	neg	neg	neg	neg
149	suganya	23	3.360	term	neg	neg	neg	neg	neg	neg
150	manju	24	2.860	term	neg	neg	neg	neg	neg	neg
151	malathi	20	3.585	term	neg	neg	neg	neg	neg	neg
152	rajeshwari	24	2.490	term sga	neg	neg	neg	neg	neg	neg
153	surya	20	2.965	term	neg	neg	neg	neg	neg	neg
154	priya	24	2.560	term	neg	neg	neg	neg	neg	neg
155	sasikala	25	2.880	term	neg	neg	neg	neg	neg	neg

156	selvi	20	2.645	term	neg	neg	neg	neg	neg	neg
157	priya	24	3.200	term	neg	neg	neg	neg	neg	neg
158	gangadevi	28	2.490	term sga	neg	neg	neg	neg	neg	neg
159	vijayalakshmi	25	2.810	term	neg	neg	neg	neg	neg	neg
160	rajabnisha	30	2.500	term	neg	neg	neg	neg	neg	neg
161	suganya	23	3.325	term	neg	neg	neg	neg	neg	neg
162	jayachitra	21	2.330	term sga	neg	neg	neg	neg	neg	neg
163	uma	23	2.465	term sga	neg	neg	neg	neg	neg	neg
164	indhumathy	23	2.600	term	neg	neg	neg	neg	neg	neg
165	malliga	28	2.660	term	neg	neg	neg	neg	neg	neg
166	priya	21	3.105	term	neg	neg	neg	neg	neg	neg
167	ponmalar	30	2.715	term	neg	neg	neg	neg	neg	neg
168	preethi	29	2.700	term	neg	neg	neg	neg	neg	neg
169	vinitha	21	3.005	term	neg	neg	neg	neg	neg	neg
170	kokilakshmi	24	3.275	term	neg	neg	neg	neg	neg	neg
171	maheshwari	29	3.340	term	neg	neg	neg	neg	neg	neg
172	sivaranjani	23	2.580	term	neg	neg	neg	neg	neg	neg
173	divya	23	2.900	term	neg	neg	neg	neg	neg	neg
174	arokayamary	35	3.030	term	neg	neg	neg	neg	neg	neg
175	susila	26	2.985	term	neg	neg	neg	neg	neg	neg
176	uma	34	1.930	preterm	neg	neg	neg	neg	neg	neg
177	velankani	19	1.900	term sga	neg	neg	pos	pos	neg	neg
178	vaidhegi	21	2.065	preterm	neg	neg	pos	neg	neg	neg
179	lavanya	27	2.010	term sga	neg	neg	pos	neg	neg	neg
180	rahamth	30	2.000	preterm	neg	neg	pos	neg	neg	neg
181	soundarya	21	2.140	preterm	neg	neg	pos	pos	neg	neg
182	lakshmi	28	3.580	term	neg	neg	pos	neg	neg	neg
183	indhra	26	1.340	preterm	neg	neg	pos	neg	neg	neg
184	susila	22	2.120	preterm	neg	neg	pos	neg	neg	neg
185	tamilselvi	25	2.830	term	neg	neg	pos	neg	neg	neg
186	rajeshwari	24	2.215	term sga	neg	neg	pos	neg	neg	neg
187	prema	22	2.125	term sga	neg	neg	pos	neg	neg	neg
188	varalakshmi	22	1.645	preterm	neg	neg	pos	neg	neg	neg
189	praveena	22	2.540	term	neg	neg	pos	neg	neg	neg
190	jini	30	2.100	term sga	neg	neg	pos	neg	neg	neg

KEY TO MASTER CHART

S no	:	Serial number
Hb	:	Haemoglobin levels
MOD	:	Mode of delivery
LMP	:	Last menstrual period
EDD	:	Expected date of delivery
DOD	:	Date of delivery
BW	:	Birth weight
GA	:	Gestational age
MR	:	Mother’s blood RDT result
MP	:	Mother’s blood peripheral smear result
PR	:	Placental sample RDT result
PP	:	Placental sample peripheral smear result
BR	:	Baby blood RDT result
BP	:	Baby blood peripheral smear result
neg	:	Negative
pos	:	Positive
nr	:	not reactive
ln	:	labour natural
lscs	:	caesarean section
SGA	:	small for gestational age
nk	:	not known