Malaria And Pregnancy

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Objectives

1. General Introduction
2. Life cycle of Plasmodium falciparum
3. Pattern of Immunity to malaria
4. Effects of malaria during pregnancy, labour and puerperium.
5. Effects of malaria on the course of pregnancy
6. Treatment of MIP – Current trend.
7. Conclusions
Introduction (1)

1. Malaria is caused by *Plasmodium* spp.
2. Vector = Female *Anopheles* mosquito
3. Endemic in Africa; S.E. Asia; Central America
4. Origin:
   Central Africa: 5,000 – 10,000 years ago.
   Deforestation for Agricultural purposes.
   Emergence of *Anopheles gambiae*
Introduction (2)

Burden of the Disease:

- 2 billion people affected worldwide.
- 2-2.5 million deaths annually (mostly pregnant women, infants 0-5 years and HIV patients; 800,000 in children 0-5 years).
- *Plasmodium falciparum* is cause of the most severe forms of malaria. Malaria is currently the most common parasitic infection.
- Greatest challenge today is Resistance to Drugs.
Life Cycle (1)

1. Sexual Reproduction (In the Mosquito)

- Transformation of male and female gametes of Plasmodium falciparum to sporozoites within salivary glands and stomach of female Anopheles mosquito.
- Duration of process: 2 weeks.
Life Cycle (2)

2. Pre-(Exo-) Erythrocytic Phase:

- Following a mosquito bite, the injected sporozoites head for the human liver via the blood stream.
- During the next 10-15 days within the liver hepatocytes, the sporozoites are transformed into merozoites.
3. **Erythrocytic Phase (Asexual Reproduction):**

- Merozoites leave the liver hepatocytes to invade the red blood cells.
- **Schizogony** = Transformation of Merozoites to Schizonts.
- **Duration of Schizogony:**
  - 36-48 hours (P. falciparum).
  - 48 hours (P. ovale/ vivax).
  - 72 hours (P. malariae).
4. **Post Erythrocytic Phase:**

- Rupture of RBCs leads to the release of transformed schizonts as male and female gametes into the bloodstream, where they cause the symptoms of malaria (fever, rigors etc).
- Rupture of RBCs occur when the concentration of Schizonts within the RBCs reach a critical minimum. The RBCs rupture in synchrony and produce the clinical symptoms of malaria.
Patterns of Immunity to Malaria (1)

1. At the Community level:

Epidemiologists describe 2 patterns:

- **Stable Immunity (occurs in holo-endemic areas):**
  1. Malaria occurs throughout the year.
  2. Community immunity is very high.
  3. Epidemics are rare.
  (Full immunity is developed by age of 7 years).
Patterns of Immunity to Malaria (2)

- **Unstable immunity:**
  1. Infection/Transmission is intermittent (e.g. 3 months in a year).
  2. Community immunity is very low.
  3. Epidemics are frequent.

(Full immunity is cannot be developed).
Patterns of Immunity to Malaria (3)

2. **At the level of the Individual:**
   - **Cellular Immunity:**
     Mediated through macrophages of the RES resulting in phagocytosis of plasmodium infected RBCs thus removing them from circulation.
Humoral Immunity:
Mediated by specific antibodies (IgG and IgM) against the Erythrocytic phase of the infection.
Factors influencing the Extent to which Individual Immunity can be developed:

1. Racial Factor (Phylogeny): e.g. Negroes and resistance against P. vivax.
2. Transmitted (Passive): short lasting (usually about a month); waxes and wanes.
3. Acquired (Active Immunity): Following repeated infections at very high cost. The extent increases with Age and Parity.

Therefore, severity of malaria depends on duration of stay and the endemicity of the area.
Immunity Against MIP

Reduction in the rate of gamma globulin synthesis in conditions of stress. Therefore.

• Parasite density increases.
• Increased tendency for dormant exo-erythrocytic infections to manifest clinically.
• Constitutional disturbances reminiscent of childhood status re-emerge: (Frequent febrile illnesses especially in last trimester); preterm labour and tendency to occurrence of severe forms of malaria e.g. cerebral malaria).
Effects of Malaria (1)

General pattern:
- General decline in immunity (most marked in first pregnancy and particularly in the third trimester).
- Pregnancy may be interrupted.
- Maternal and/or fetal death may occur.

(However, these effects become less pronounced with increasing parity).
Effects of Malaria (2)

During Pregnancy (1):

- Frequency and severity of attacks increase.
- Rapid installation of anaemia (due to haemolysis and sequestration of infected RBCs into the RES).
  
  (Even non-parasitized rbc's may be opsonized and develop auto-antibodies that make them prone to haemolysis. Such opsonized rbc's are sequestrated into the spleen and removed from circulation by lympho-macrophages).
Effects of Malaria (3)

During Pregnancy (2):
- Potential anaemia patients are young primigravidae with hepato-splenomegaly.
- Appearance of megaloblastic changes in the bone marrows.
- Maternal and/or fetal death may occur.
  (However, these effects become less pronounced with increasing parity).
Effects of Malaria (4)

During Labour:

- Further stress occurs with tendency for clinical malaria to occur. Treatment must be via parenteral route.
- If clinical state is poor, the second stage must be by the use of either forceps or ventouse.
- Any PPH may be fatal.
- Heart Failure can occur in the immediate post partum.
Effects of Malaria (5)

During The Puerperium:

- Further stress occurs with increased tendency for sub-clinical malaria to become clinical.
- Therefore to prevent relapse, ‘prophylaxis’ should be continued until 6 weeks postpartum.
- Lactation is not usually disturbed except in cases of severe pre-existing anaemia.
Effects of Malaria on the Course of Pregnancy (1)

1. Pyrexia can induce Uterine Contractions:
   - Abortions.
   - Preterm labours.
   - Intra-Uterine Growth Retardation (IUGR).
   - Intra-Uterine Deaths.
   - Stillbirths.
Effects of Malaria on the Course of Pregnancy (2)

2. Placental Parasitization:

The placenta acts as a spleen because of clogging of the intervillous spaces with macrophages (Placental Reaction), which is most marked during the second half of pregnancy:

- The extent of placental reaction is proportional to the severity of malarial infection during pregnancy.
Effects of Malaria on the Course of Pregnancy (3)

- More common in well-immuned women with frequent parasitaemia but little constitutional disturbances and in first pregnancies (when compared with higher order pregnancies).
- Ultimate Effect of Placental Parasitization: IUGR, LBW and IUD.
Effects of Malaria on the Course of Pregnancy (4)

Effects of Placental Infection:

1. Transplacental passive immunity (IgG) protects newborns against developing congenital anaemia, provided maternal immunity is high.

2. Low maternal immune status offers no protection against development of congenital anaemia. Therefore, such babies may be stillborn or suffer ENND.
TREATMENT OF MIP (1)

Preamble (1):

1. CQ has been first line drug for long.
2. Resistance to CQ has developed worldwide in past few decades:
   - Climatic changes
   - Industrialisation

Have led to changes in the ecosystems of vectors resulting in the development of resistant strains of Plasmodium.
TREATMENT OF MIP (2)

Preamble (Cont’d):

1. Emergence of mutant strains in past 20 years have resulted in a doubling of malaria-related death rates worldwide (2-2.5 million deaths annually among pregnant women, children 0-5 years and adults with HIV infection; currently there are 800,000 deaths annually among children 0-5 years).

2. Despite reported resistance to CQ in almost all countries in tropical Africa between 1978 and 1988, CQ still remains the first line drug in most countries.
Preamble (Cont’d):

3. The Abuja Declaration of April 2000, on the concept of ‘Roll Back Malaria’ aims at reducing malaria-related deaths among pregnant women and children 0-5 years by 60% by the year 2010.

4. The Tripod Principles of RBM are:
   - Use of insecticide-impregnated nets (ITN).
   - Use of Intermittent Presumptive Treatment (IPT) during pregnancy.
   - Early diagnosis and prompt treatment of cases.
The Problem of Drug Resistance:

1. WHO recommends Sulfadoxine-Pyrimethamine (S-P) or Amodiaquine (Camoquine) for IPT regimes during pregnancy.

2. Whenever the level of resistance to CQ reaches 15%, WHO recommends the use of drug combinations.
TREATMENT OF MIP (5)

WHO Criteria for Drug Combinations:

1. The chosen combination must be effective. This overall efficacy must be independent of the efficacy of the individual components.

2. Must be able to delay the emergence of drug resistance.

3. Can be used by a wide range of people in any chosen community, especially the population at risk.

4. Its instructions for use should be sufficiently simple even for home use by the general population.

5. High degree of compliance.

6. Must be cost-effective i.e. Availability and Accessability.
WHO Recommendation for the sub-Region:

- **IPT during Pregnancy: S-P (Fansidar) and Amodiaquine (Camoquine).**
- **General Population: Coartem.**

**Composition:** Artemisine derivative and Lumefantrine.
Recommendations of the Cameroon MOH:

- **IPT during Pregnancy**: S-P (Fansidar) and Amodiaquine (Camoquine).
- **Case treatment during pregnancy**: Parenteral Quinine.
- **General Population**: To be available in 2 years. Composition: Artemisine and Amodiaquine.