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A REVIEW OF PARASITIC INFESTATION IN PREGNANCY

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ABSTRACT

Infection with pathogenic protozoa exerts an enormous toll on human suffering, notably but not exclusively in the tropics. The most important of the life threatening protozoal diseases is malaria, which is responsible for at least one million deaths annually, mostly in young children in developing countries. Pathogenic parasites are generally classified into four types: sporozoa, amoebae, flagellates, and others.

Most of these organisms cause infections by being ingested in the form of eggs or larvae, usually present on contaminated food or clothing, while others gain entry through skin abrasions or by mosquito bite. Common parasitic infestations in pregnancy include malaria, hookworm, amoebiasis and tapeworm infestations. Once in the body, parasitic worms may go unnoticed if they cause no severe symptoms. However, if they multiply rapidly and spread to a major organ, they can cause very serious and even life-threatening conditions. Pregnancy can be disrupted at the maternal, fetal and placental levels by parasitic infestations.

The diagnosis of intestinal nematodes is usually made after demonstration of eggs in the faeces or passage of the worms themselves, or in the case of malaria by blood film.

Antihelminthic drugs are prescribed to treat these infestations. They function either by destroying the worms on contact or paralyzing them, or by altering the permeability of their plasma membranes. The dead worms then pass out of the body in the faeces. Most pregnant patients with intestinal parasite infections may be managed without anti parasitic chemotherapy.

There is research evidence reporting that some antihelminthic drugs cause birth defects or miscarriage in animal studies. However, no human birth defects have been reported with antihelminthic drugs.

Parasitic infections in pregnancy directly or indirectly lead to a spectrum of adverse maternal and fetal outcomes, and effects on the placenta. Their consequences in chronically under nourished or anaemic women of reproductive-age are considerable.

Keywords: Parasites, Pregnancy, Treatment, Pregnancy Complications.

INTRODUCTION

Parasitic diseases caused by helminthes and protozoa are major causes of human disease and misery in most countries of the tropics. The burden due to soil-transmitted helminthes (STH) and schistosome infections is enormous. More than 40% of tropical disease burdens, excluding malaria, are due to this group of infections. Over two billion people are affected worldwide, of whom more than 300 million suffer from associated severe morbidity: Taken together, STH and schistosome infections are the most prevalent parasitic infections in the world [1]. Poorer families are perpetually those who suffer the most, and within that group

adolescent girls and pregnant women - all at critical phases of life- are put among the highest risk. The impact in terms of individual suffering is silently devastating, while in economic terms the productivity of entire countries is dampened [2].

Parasitic infections affect tens of millions of pregnant women worldwide, and directly or indirectly lead to a spectrum of adverse maternal and fetal/placental effects. Pregnant women often experience more severe infections than their non-pregnant counterparts [3]. Among parasitic infections, malaria and intestinal helminthes coexist widely with micronutrient deficiencies, and contribute importantly to anaemia and a cycle of retarded growth and development. In somewhat more limited or focal geographic settings, other parasitic diseases (e.g., schistosomiasis, filariasis) contribute similarly to this cycle [4].

Paradoxically, many of these parasitic infections have been forgotten; they have become the 'neglected diseases', often overlooked and rarely a high priority. This review will concentrate more on such diseases.

EPIDEMIOLOGY & PATHOPHYSIOLOGY

Generally, pathogenic parasites are divided into four groups. 1. Sporozoa - this group includes the malaria parasite and the related coccidiosis (Toxoplasma Gondii). 2. Amoebae – the most important parasite in this group is Entoameba histolytica. 3. The flagellates - this includes trichomonas vaginalis, Giardia lamblia, and others. 4. The trypanosomes - rarely seen nowadays. Women who are infected with one parasite are usually infected with a second and sometimes a third parasite. This is especially true with helminthes and malarial infection [3]. Almost every parasite either directly or indirectly causes anaemia and malnutrition. Both anaemia and malnutrition are associated with an increased incidence of adverse pregnancy outcomes [4]. Infection occurring during the first trimester is associated with more severe fetal and placental consequences than those occurring later in pregnancy. Maternal infection is often more severe in the primagravida, and tends to result in a higher degree of parasitemia. Incidentally, the natural immune response to pregnancy causes women to be more susceptible to parasitic infections when pregnant than in the non-pregnant state [5].

Malaria is the most important parasitic infection in humans, transmitted by the bite of the sporozoite-bearing female anopheles mosquito; it is the tropical disease most commonly imported from the endemic areas of the world to the West. There are four types of malarial parasite, viz: plasmodium falciparum, P vivax, P malariea, and P ovale. The effect of malaria infection results from systemic infection comparable to any severe febrile illness in pregnancy. In the mother it leads to miscarriage, premature birth, intra-uterine growth restriction (IUGR), still birth, and both maternal and fetal anaemia.

Vertical transmission to the fetus can occur with malaria at the time of birth. All neonates whose mothers developed malaria during pregnancy should be screened for malaria with standard microscopy of thick and thin blood smears at birth, and weekly blood smears for 28 days[4] . The reported incidence of congenital malaria varies from 8–33%. In non-endemic regions, malaria should be treated by a multidisciplinary team, and advice should be sought early enough from an infectious diseases specialist. Delay in diagnosis and treatment may lead to death in severe malaria.

Intestinal worm infections are common worldwide, but thrive in poor communities in the tropics, where poor water supply and poor sanitation are common. The burden of infection is estimated to exceed 100 million infected persons each year for roundworm (Ascaris lumbricoides), hookworm (Ancylostoma duodenal and Necator americanus) and whipworm (Trichuris trichiura)[6]. Hookworm infection causes mechanical laceration and enzymatic

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damage to the mucosa of the small intestine, leaving behind small bleeding lesions; leading to approximately 0.05 mL/d of blood loss per adult Necatur americanus, and approximately 0.25 mL/d per adult Ancyclostoma duodenale[7]. Hypochromic microcytic anaemia (iron deficiency anaemia) follows chronic infection within 3–5 months after exposure. These infections may predominate in young and school-age children, but their consequences in chronic under nutrition and anaemia in reproductive-age women is considerable. The gastrointestinal blood loss, malabsorption and appetite inhibition may further aggravate the iron, zinc and protein-energy deficiencies and anaemia of pregnancy.

Humans develop ascariasis by ingesting the eggs of Ascaris lumbricoides. These eggs hatch and the larvae migrate through the gut walls into the bloodstream and then to the lungs. Once in the lungs they move up the trachea, are swallowed, and then mature to adulthood in the small intestines. They can grow to sizes of greater than 25 cm and lay more than 200,000 eggs daily [7].

Schistosomiasis, principally caused by S. haematobium, S. japonicum and S. mansoni, is endemic in 74 countries and infects more than 200 million people worldwide [8]. Women of reproductive age may experience genital tract infection, with disease in the pelvis affecting the renal system and the genital tract, including salpingitis and tubal obstruction with possible ectopic pregnancy. As a systemic disease that causes anaemia, schistosomiasis may have consequences similar to those described for hookworm infection. Some case reports of congenital infection exist, and S. haematobium eggs have been identified in placental blood [8].

Filariasis is endemic in more than 80 countries, and an estimated 120 million people are infected (two-thirds of infected people are in India and sub-Saharan Africa) [9]. This blood-born parasite leads to local inflammation with lymph node involvement, including in the pelvis, and possibly affecting reproductive organs.

African trypanosomiasis (sleeping sickness caused by Trypanosoma gambiense or T. rhondesiensi) and American trypanosomiasis (Chagas disease caused by T. cruzi) affect substantial populations on their respective continents, and can infect women during pregnancy and lead to congenital infection of the newborn[4].

CLINICAL MANIFESTATION

Pregnancy can be disrupted at the maternal, fetal and placental levels by parasitic infestations. Malaria may infect the placenta, leading to maternal anaemia, spontaneous abortion, stillbirth and low birth weight. Malaria parasites may cross the placenta, particularly in non-immune mothers, leading to congenital malaria [28]. The placentas from patients treated for malaria should always be examined histologically (though this may not be possible in malarial areas) for the presence of parasites. If these are present, the neonate is at risk, and should be on a course of antimalarial therapy.

Hookworm adheres to the intestinal mucosa and extracts blood and nutrients, leading to anaemia and malnutrition [10]. Severe maternal anaemia and malnutrition are associated with fetal growth restriction and low–birth weight (LBW) infants [11].

Infections with Ascaris Lumbricoides are asymptomatic initially. However, as the burden of infection increases, abdominal pain, pulmonary symptoms, and anaemia may become more severe. The acute phase of the infection is characterized by fever, cough, and pulmonary congestion [12]. As in their non-pregnant counterparts, pancreatitis, biliary obstruction, and intestinal obstruction have all been noted in gravid women, with biliary obstruction being the most common complication [14]. The gravid female is thought to be more prone to biliary

Ascaris infection because progesterone alters/relaxes the motility of the sphincter of Oddi. Biliary infection is also most commonly seen in the third trimester, as levels of progesterone rise. Ascaris' coagulopathic properties (increased clotting and partial thromboplastin time) may play a role in post-partum haemorrhage[13,14].

Acute infection with Schistosoma is usually subclinical, causing mild anaemia. However, chronic infection can lead to granuloma formation and a fibrotic tissue response. It is this aggressive immune response that leads to clinical pathology. Granulomas may lead to portal hypertension, pulmonary hypertension, and cystitis, and even bladder cancer. Schistosome eggs and subsequent granuloma formation are known to cause tumors/ulcers in the lower genital tract leading to dyspareunia. Tubal granulomas affect tubal motility and patency, and are associated with infertility and ectopic pregnancy [15]. Schistosoma can infect the placenta and the fetus and may lead to IUGR, LBW, preterm labour and still birth.

Visceral leishmaniasis (Kala-azar) is cause by Leishmania Chagasi. It infects the bone marrow and spleen preferentially, in addition to the mucous membranes or skin. Symptoms include fever, weight loss, anaemia, hepatosplenomegaly, pancytopenia, and hyperpigmentation of the skin [16]. L. Chagasi and L. Donovani may cross the placenta. Multiple case reports discuss infected women giving birth to infected infants, and to infants with disseminated disease (in thymus, lungs, kidneys, and placenta). Untreated cases are linked with spontaneous pregnancy loss as well as active newborn disease [16].

Filariasis has acute and chronic phases. The acute phase is caused by a microfilaremia (filarial larvae infection in the bloodstream) and is associated with relapsing fever, lymphedema, skin inflammation, and malaise. However, it is the chronic phase that causes significant morbidity. The parasite migrates toward the vessels in the legs and pelvis, causing severe lymph varices and elephantiasis over time [17].

DIAGNOSIS

Diagnosis of intestinal nematodes is usually made after demonstration of eggs in the faeces or passage of the worms themselves. This parasitological study is either by direct wet-mount, a formaldehyde-ether sedimentation method or modified acid-fast staining techniques [10].

Abdominal ultrasound is the ideal modality to identify and diagnose Ascaris infection in the pregnant female. On abdominal ultrasound, Ascaris infection (in any viscera) is characterised by the "railroad sign" in longitudinal view and the "bull's-eye sign" in cross section[18]. The worms can also be seen as moving linear echogenic foci. Laboratory findings in Ascaris infection may include a mild eosinophilia as well as a prolonged prothrombin time, clotting time, and partial thromboplastin time[19].

Diagnosis of schistosomiasis is made by demonstration of eggs in the urine or faeces. Proinflammatory cytokines (TNF-α , IFN-δ) are usually elevated[20]. Diagnosis of leishmaniasis is usually made based on clinical grounds. There are serologic tests available in endemic areas [10].

Diagnosis of Trypanesomiasis is made based on demonstration of trypomastigotes in the blood or tissues, a positive polymerase chain reaction result, or serologic tests. Thick blood films with Giemsa stain are most commonly used to confirm blood or tissue infection [10].

Filariasis is diagnosed by microscopic visualization of parasites from blood or tissue samples.

Diagnosis of malaria is by species identification. Microscopy and rapid diagnostic testing are the standard tools available - microscopic examination of thin and thick films.

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TREATMENT

There is research evidence reporting that some antihelminthic drugs cause birth defects or miscarriage in animal studies. However, no human birth defects have been reported [27] .

Some antihelminthic drugs can pass into breast milk. Breastfeeding may have to be discontinued until the antihelminthic treatment has ended, and breastfeeding mothers must also inform the prescribing physician.

Intestinal nematodes are easily treated with albendazole, which has been shown to be more efficacious than mebendazole in multiple trials[21]. Both mebendazole and albendazole are category C agents, but are generally considered safe in the second and third trimester [12]. WHO guidelines recommend prophylactic antihelmintic agents be included in routine antenatal care in areas where hookworm prevalence is greater than 20% to 30%. Oral iron supplementation is also recommended in these patients [11]. When intestinal obstruction occurs during Ascaris infection, surgery or colonoscopy is an option. Endoscopic retrograde cholangiopancreatography (ERCP) has been effective in treating biliary ascariasis[22]. Schistosomoiasis is treated with praziquantel: 20mg/kg to be repeated after 4 hours.

The drug of choice for treating leishmaniasis is a pentavalent antimonial compound, meglumine antimonite, for 20 to 40 days, but is contraindicated in pregnancy. Amphotericin B is the second-line drug, which is considered safe and effective in pregnancy[16]. Treatment of Chaga's disease with nifurtimoxor benznidazole is recommended in the acute, subacute, and chronic phases. However, there are no clear data demonstrating the safety of nifurtimox or benznidazole during pregnancy [11].Treatment of filariasis with diethylcarbamazine and albendazole has been shown to be effective acutely, as well as to decrease progression to chronic disease [23].

Malaria during pregnancy should be treated as an emergency. Treatment depends on the local area, the dominant plasmodium type and the pattern of drug resistance. The patient may need to be admitted, while in some cases severe complicated malaria may even require admission to an intensive-care unit (ICU), especially in non-endemic areas. For ordinary malaria, ART may be sufficient, while severe falciparum malaria may require intravenous artesunate or quinine. Quinine does not increase the risk of preterm labour, but in pregnancy in particular, patients are at risk from quinine-induced-hyperinsulinemia, which can cause fatal hypoglycemia. 50% dextrose should be used; where this is not effective, somatostatin analogues such as SMS-201-99525 which inhibit insulin release are the treatment of choice for quinine induced hypoglycaemia. Many malarial parasites in the tropics are resistant to chloroquine [27].

PREVENTION

The World Health Organization (WHO) recommends five public-health strategies for the prevention and control of NTDs: preventive chemotherapy; intensified case-management; vector control; provision of safe water, sanitation and hygiene; and veterinary public health (that is, applying veterinary sciences to ensure the health and well-being of humans)[1].

Efforts to control hookworm infection include the sanitary disposal of faeces and educational campaigns about the proper use of latrines. At this time, the most cost effective way to control hookworm infection has been through population wide treatment with either albendazole or mebendazole. However, reinfection usually occurs within a few months after deparasitazation, which means repeated or frequent use of the drug. This may lead to drug resistance. Therefore, a safe and cost-effective vaccine would provide an important new tool for the control of hookworm infection.

There is a global elimination strategy for filariasis which consists of two components [24]. The first is annual mass drug administration; the second is reducing the impact on patients with the chronic forms of the disease, elephantiasis or hydrocele. Recent evidence has shown that regular cleansing and treatment of the affected areas with antibiotic ointments can substantially reduce super infection of the skin in the affected areas, and thereby limit the extent of lymphoedema. This simple procedure has been shown to improve the quality of life substantially for those with the severe disfiguring form of the disease. Although the tools to eliminate lymphatic filariasis already exist, in many endemic countries the disease is not considered a priority, so it is often difficult to generate the political commitment to mount an effective elimination programme.

Fansidar has been used for malaria prophylaxis in high-risk areas with good results [25, 26]. The current practice is to give two doses in pregnancy during the second trimester four weeks apart, except in HIV patients where three doses are recommended. In low-risk areas, malaria prophylaxis with chloroquine or proguanil should be continued throughout pregnancy, and visitors to holoendemic areas should continue with their prophylaxis for at least the last trimester and preferably until delivery.[27,28]

Attempts to develop vaccines against most of the parasites discussed have been hampered by difficulties in cultivating them in vitro, and the complexity of their multicellular Organisation and/or multistage development, added to their impressive antigenic variability. Although remarkable progress has been made over the last decade in the cloning and expression of protective antigens from a large number of parasites, the prospect of using these antigens for the development of protective vaccines has met with little enthusiasm from industrial vaccine manufacturers [24].

CONCLUSION

Parasitic infections in pregnancy directly or indirectly lead to a spectrum of adverse maternal/fetal outcomes and placental effects. Their consequences in chronically under nourished and anaemic women of reproductive-age are considerable. The gastrointestinal blood loss, malabsorption and appetite inhibition may cause or further aggravate iron, zinc and protein-energy deficiencies, and the anaemia of pregnancy. Improved environmental sanitation, provision of portable water supply and sanitary sewage disposal facilities; coupled with administration of prophylactic antihelminthic agents to pregnant women in areas of high prevalence, are important in preventing infestation by these parasites. More global attention to the diagnosis and treatment of parasitic infections in pregnancy is warranted.

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