Review Article

Notions about pregnancy and parasitic diseases

Abstract

In pregnant women, parasitic diseases constitute an important public health problem due to physiological factors that characterize this stage. That is why it is crucial to review different aspects of the parasite-host interaction as tools for the prevention and control of these pathologies during pregnancy, the objective of this paper. This is a documentary-type investigation. The information obtained was grouped into 6 chapters: resistance or susceptibility of pregnant women to parasitic diseases, anemia and parasitic diseases in pregnant women, relationship between micronutrient deficiency and parasite infection in pregnant women, congenital transmission of parasites, treatment of some parasitosis in pregnant, and conclusions.

Keywords: pregnancy, parasitic diseases, parasite, immune system

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Introduction

Parasitic diseases are of great importance as a public health problem, especially in groups of populations with associated physiological risk factors such as pregnant women, therefore, they require greater health care to avoid maternal and fetal complications, such as anemia (aggravated with some parasitic diseases) that affects severely in women and in embryonic and fetal development,[1] that is why it is crucial to review knowledge about different aspects of parasite-host interaction, complications of parasitosis and treatment of them in pregnant women, as elements crucial to take into account in the prevention and control of these infections and diseases in such a vulnerable population group, fundamental objective of this writing.

Methodology

The present research work was of a documentary type based on the review of manuscripts, for which the databases such as: Pubmed, Medline, Scopus, Lilacs, Science Direct, SciELO and Ovid were used. Descriptors were used in the search. The resulting information was grouped into 6 chapters: resistance or susceptibility of pregnant women to parasitic diseases, anemia and parasitic diseases in pregnant women, relationship between micronutrient deficiency and parasite infection in pregnant women, congenital transmission of parasites, treatment of some parasitosis in pregnant, and culminates with some conclusions on the subject developed.

Resistance or susceptibility of the pregnant woman to parasitic diseases

The levels of sexual steroid hormones (estradiol and progesterone) and protein type (gonadotropins, oxytocin and prolactin, among others) as participants in the regulation of pregnancy, are also involved in the susceptibility or resistance of the pregnant woman to some parasitic diseases, in a fine interaction between the endocrine and immune systems.[2] It is also pointed out that the cells in the endometrium in the non-pregnant are highly immune, so that they reach up to 30% of the total cells that comprise it, mainly natural killer cells (NK), macrophages and T lymphocytes, cells that could prevent embryo implantation, an effect counteracted by the specific suppression of its activity in pregnant women.[3–8]

The immune suppression during pregnancy, called by experts the "receptivity window" due to the change observed in the immune microenvironment of the endometrium in favor of embryo implantation

as a direct consequence of the decrease in the populations of immune cells is explained by two mechanisms, the first, by the apoptosis of the cells that initiate cellular immunity (monocytes and macrophages) by the action of sex steroids (17-β estradiol and progesterone), accompanied by the increase in the production of interleukins 4 and 10, with the involvement of leukocyte migration inhibitory factor and monocyte colony stimulating factor;[3,7,9,10] the second mechanism refers to the polarization of cellular immunity to the humoral, that is, from Th1 to Th2,[11,12] also due to the effect of sex steroids, through the activation of the progesterone pathway of STAT-6, thus promoting the transcription of IL-4, IL-10 and TGF-β, cytosines that inhibit the Th-1 response and promote Th-2 type response.

In this order of ideas, the susceptibility of the pregnant woman to parasitic infections is modulated by the endocrine and immune systems, of course with the participation of the parasite, in this sense it is understood that the parasite load or parasitaemia is decisive for the success of the infection, that the parasite can migrate to target organs (Plasmodium falciparum can go to the endometrium, the decidua, placenta and umbilical cord. Also *Trypanosoma cruzi* can migrate towards the interstitium of the uterus, decidua, placenta and in aborted fetuses), which pregnant women are five times more susceptible to infection by these biological agents than nonpregnant ones, and that the embryo can be equally affected, for example *Shistosoma mansoni* and *Toxoplasma gondii* can cross the yolk sac.[4,13–18]

Likewise, the Th2-type immune response that guarantees fetal survival in the pregnant woman, increases her susceptibility to parasitic infections dependent on the Th1-type immune response, among them leishmaniosis, so the increase in parasitaemia is correlated with decrease IL-2 and INF-γ (Th-1 immunity).[19,20] The phase-dependent steroid hormones during pregnancy can be altered in their concentration by the action of parasitic infections such as the one triggered by *Schistosoma mansoni*, in this sense it is observed that as the parasite load increases, so do testosterone levels, while decreasing significantly those of progesterone and estradiol. Likewise, it has been found in pigs that the prevalence of *Taenia solium* infection increases markedly in pregnant women compared to non-pregnant women.[21]

After the infection is established in pregnant women, multiple immuno-endocrine factors intervene in the facilitation or restriction of the development of the parasite in the host, for example, *Taenia crassiceps* causing murine cysticercosis in vitro tests with estradiol and progesterone, its reproduction is increased, create through binding

of the steroid to a nuclear receptor of the parasite.[2,22] In malaria in pregnant women, due to its lower Th2 response, the parasite density is higher, particularly in the second trimester of pregnancy, and it is also known that with parity, the immune response increases. In relation to the fetus, it is known that the immune response is diminished and that the infected red blood cells are sequestered in the intervillous space of the placenta with an inflammatory response of monocytes, these circumstances contribute to the stimulation of premature labor and retardation of intrauterine growth, the latter This event is attributed to the consumption of nutrients and oxygen by the parasites that cause malaria and the increase in thickness that they cause in the cytotrophoblastic membrane with impaired nutrient transport. The risk of fetal malarial infection during labor is also higher, due to the presence of these parasites in the placenta.[1,23]

Anemia and parasitic diseases in pregnant women

A third of the global burden of anemia is attributed to parasitic diseases such as malaria, hookworm, and schistosomiosis. In pregnant women, the risk of anemia due to parasitic disease is increased by the disproportionate increase in plasma volume with respect to the concentration of erythrocytes (a phenomenon known as hemodilution), a very serious matter in this population group because anemia is associated with increased risk. of maternal mortality, premature delivery, low birth weight and perinatal mortality.[24,25] Parasites by multiple pathways and mechanisms can cause or aggravate anemia, for example, by reduced appetite (this compromises nutrient intake), by intestinal blood loss, by deterioration of the intestinal lining and by interference with absorption that induces Inflammation, however, the effect of parasites on anemia of the pregnant woman, requires further and deeper investigations.[26–28]

Pregnant women in developing countries frequently suffer from malnutrition and recurrent infections that can end in severe sequelae that generally continue for generations to come. In relation to infections, parasitic diseases occupy a prominent place in the generation of anemia, with malaria and schistosomiosis as their main representatives, without this meaning that other parasites of lower prevalence can also contribute to low levels of hemoglobin in pregnant women.[28] In malaria, anemia may be due to hemolysis of erythrocytes and their sequestration in the placental bed by the action of *Plasmodium spp*. Of the malaria-causing parasites Plasmodium falciparum is the most common,[29] therefore, it is recommended that together with antimalarial drugs, iron, folate and vitamin A supplements be administered to pregnant pregnant women.[23,30,31]

There is a clear association between infection by intestinal parasites and anemia that can be explained in hookworm due to blood loss due to mechanical laceration and the enzymatic damage caused by these hosts in the human intestinal tract, for example with *Necator americanus* 0.05mL/day of blood volume per adult parasite and with *Ancyclostoma duodenale* 0.25mL/day, which after a period of 3 to 5 months with the infection ends in hypochromic microcytic anemia, this is particularly alarming in pregnant women because it is estimated that 44 million of them (of approximately 144 million) suffer from hookworm.[32,33] Other parasitoses can also cause anemia in the pregnant woman, in this sense schistosomiosis (mainly *Schistosoma haematobium*, *S. japonicum* and *S. mansoni*) is mentioned, which is also capable of producing infection in the genito-urinary tract and leading to salpingitis, tubal obstruction and possible ectopic pregnancy that is to cause reported anemia in this group of women.[23,27,34]

Relationship between micronutrient deficiency and parasite infection in pregnant women

There is a consistent relationship between micronutrient deficiency and parasitic infection in pregnant women, this is not exclusive to this population group, but common to the entire population, but in them the increased demand for micronutrients exacerbates the deficiency, therefore, the risk of parasitic infection in terms of frequency and intensity. The main micronutrients mentioned in the interaction with the parasitic infection are vitamins A, C and E, vitamin B12 (riboflavin), folic acid, iron and zinc. In the case of vitamin A, its deficiency affects the synthesis of retinol that intervenes in the production of acute phase reactants (C-reactive protein, plasminogen, complement factors, among others) that are activated in response to inflammation and damage tissue. Vitamin C deficiency implies failure of T lymphocyte response and complement function and phagocytosis.[35–37]

Deficiencies in the availability of vitamin E, iron and Zinc translates into defects in cellular and humoral immune responses that include altered cytokine function and reduced phagocytic function. However, vitamin B deficiency seems to influence the multiplication and growth of the malaria parasite by mechanisms that are not yet very clear. Likewise, folate deprivation protects against malaria by altering metabolism in species of this group of parasites.[35–37]

Congenital transmission of parasites

The intrauterine passage of parasites from the pregnant woman to the product of conception is what is defined as congenital transmission or intrauterine infection. Congenital transmission is possible without the pregnant woman showing the clinical signs and symptoms of the disease; it is enough for her to be infected, as is the case with Chagas disease. In the definition of congenital transmission, the passage of parasites to the newborn through breast milk must be ruled out, as is the case with *Trypanosoma cruzi*, Toxoplasma gondii and malaria parasites.[38–40]

Virulence and tropism directly affect congenital transmission, with respect to the first variable, high parasito ussay and acute phase loads are thought to increase the risk of infection of the conception product in uterine, although in the second variable, it is thought that frank tropism reduces the permanence of the parasite in circulation and with it the congenital transmission.[41,42] In general terms, there are two origins that congenital transmission of microorganisms can have: from circulating maternal blood or from elements retained in the uterine mucosa, in this sense, some authors believe that a continuity solution or morphological (or functional) alteration is required) of the placenta.

In *Toxoplasma gondii* there is controversy regarding the congenital transmission of this parasite, since Sabin maintains that it only occurs when the mother acquires the infection during pregnancy (acute generalized tachyzoite infection), that it does not recur in successive pregnancies and that the Intrauterine transmission only occurs from the second half of pregnancy, it can thus cause fetal disturbances and premature deliveries,[43] however, other authors postulate congenital transmission in the chronic phase of maternal toxoplasmosis (attributed to reactivation processes by rupture of tissue cysts with bradyzoites, slow reproduction forms), therefore, the transplacental passage is possible in successive pregnancies (from the fourth or fifth week), in any period of the same and embryopathies and abortions.[39]

Likewise, it is known that during the third trimester of pregnancy the probability of transplacental infection is high (65%) and its effects on the fetus are mainly related to learning disorders and chronic neurological sequelae, while during the first trimester the risk of infection is lower (15%), but the sequelae in the product of conception are more severe, including abortion and intrauterine fetal death.[44–46]

Treatment of some parasite in pregnant women

Pregnant women living in poverty are extremely vulnerable to parasitic infections, particularly those caused by soil-transmitted helminths (*Ascaris lumbricoides*, *Trichuris trichuira* and *Ancylostoma duodenalis* or *Necator Americanus*), therefore, in order to reduce the burden of infections, chemoprophylaxis with a single dose of albendazole (400mg) or mebendazole (500mg) after the first trimester of gestation, in areas with prevalence of *T. trichuira* infections equal to or greater than 20% in pregnant women and where the prevalence of anemia is equal to or greater to 40% in these, in addition, comprehensive measures must be implemented, particularly the improvement of water, sanitation and hygiene.[47]

For protozoa in pregnant women, prophylactic treatment of Plasmodium falciparum malaria is recommended due to the severe consequences it produces in the fetus (anemia, low birth weight, premature delivery and fetal death). In this sense, intermittent preventive chemotherapy is indicated with sulfadoxine and pyrimethamine at least three doses after the end of the first trimester of pregnancy accompanied by the use of window nets and mosquito nets impregnated with insecticides.[48,49]

Due to the reduced risk of transplacental infection, early treatment of toxoplasmosis is recommended in pregnant women with high IgM or IgG titers, or in those who have experienced seroconversion. The recommended drugs before 20 weeks of gestation are spiramycin (2 to 3g/day in three doses, this drug reaches high concentrations in the placenta, but not in the amniotic fluid), and after 20 weeks of gestation with pyrimethamine. (1mg/Kg/day) plus sulfadiazine (50-100mg/k weight/day, every 6 hours) and folinic acid (5-10mg daily) (if fetal infection has been diagnosed).[50–52]

Conclusion

There is a refined interaction between the endocrine and immune systems in the susceptibility or resistance of the pregnant woman towards some parasitic diseases, of course with the participation of the parasite, for example, through the parasite load and trophism. In pregnant women there is a high risk of anemia due to hemodilution, a disorder aggravated by parasites through multiple pathways and mechanisms, and parasitic infection in pregnant women also produces micronutrient deficiencies. Intrauterine passage of parasites from the pregnant woman to the product of conception is also frequent. Lastly, it should be noted that prudence must prevail in the treatment of pregnant women with parasitic diseases in observance of the specific therapy for each case, dosage, risk factors, and evaluation of benefit versus contralateral effects.

Conflicts of interest

The author and co-authors have no conflicts of interest relevant to this article.

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