

Pregnancy and the Tropics: Physiology, Environment and Infectious Disease

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Abstract

Disease processes often present and progress differently during pregnancy, often with worsening of the disease itself or adverse effects on the pregnancy. This article presents a brief overview of the physiological changes that occur with pregnancy and how they affect the pregnant patient's response to the natural environment and to infectious diseases.

Keywords: Pregnancy; Tropical disease; Physiology; Infections

Introduction

The synergy between various disease processes and pregnancy often brings a sense of confusion and discomfort to the medical provider caring for the pregnant patient, whether that be the obstetrician or the infectious disease specialist. In this article we present a brief overview of some of the interactions between various disease processes and pregnancy and some of the physiologic changes that predispose to these sometimes different presentations of otherwise well-known diseases.

Pregnancy Physiology

Immunology

During pregnancy, there are important changes that occur in the immune system. Beginning early in pregnancy there is a reduction in cell-mediated immunity. This results in increased susceptibility to a number of infections in which the cell-mediated immune response is primary. Examples of this type include malaria, amebiasis, coccidiomycosis, leishmaniasis, leprosy, listeriosis and tuberculosis [1,2]. By contrast, infections in which the humoral response is the most important show no increase in susceptibility. B lymphocyte cell numbers and functions do not appear to be reduced during pregnancy.

Vaccination

When considering vaccination during pregnancy, therefore, both safety and efficacy must be taken into account as well as the risk: benefit ratio. As high fever during the first trimester has been associated with neural tube defects precautions may be taken to prevent post-vaccination fever. In some instances there is concern that vaccination may not produce an adequate immune response, as has been observed with yellow fever and perhaps Hepatitis A vaccines [3,4]. In addition, pregnancy slows intestinal transit and may increase the risk of gastrointestinal adverse events with the use of live oral vaccines such as cholera and typhoid.

Pharmacokinetics

As with vaccination, use of medications in pregnancy requires consideration of both safety and efficacy. Many medications are absorbed, distributed and metabolized differently during pregnancy [5]. The most common outcome is a lowering of the effective serum concentration so that doses may need to be increased in order to be effective. The degree to which this occurs is neither reliable nor constant, however, so that establishing an effective drug level may require actual serum measurements or, more commonly, an empiric adjustment of dosage based on required action and side effects. Travel-related drugs may also interact with other commonly used medicines, and common mild side effects may become more pronounced. In addition, most drugs transfer across the placenta by simple diffusion and drug transfer increases with gestation due to reduced thickness of the placenta.

Venous thromboembolism

Pregnancy is a hyper coagulable state and the risk of thromboembolic disease is increased in instances such as prolonged travel or bed rest [6].

Air pollution

Air pollution, an increasingly common phenomenon worldwide, may cause more health problems during pregnancy as ciliary clearance of the bronchial tree is slowed and the mucus more abundant [7].

Sun, heat and humidity

Body temperature regulation is not as efficient during pregnancy and temperature extremes cause greater stress on the gravid women [8]. In addition, an increase in core temperature such as with heat prostration or heat stroke may be harmful to the fetus [9]. The vasodilating effect of a hot environment might also cause fainting. And, although not particularly harmful, sun exposure during pregnancy may increase chloasma, the normal, patchy skin darkening that occurs with pregnancy.

Altitude

As hyperventilation and increased cardiac output are normal in pregnancy, a pregnant woman who travels to high altitude may experience exaggerated breathlessness and palpitations [10]. Also, the common symptoms of acute mountain sickness (insomnia, headache and nausea) are frequently also associated with pregnancy and might confuse a diagnosis. In addition, diuresis may further predispose to thrombosis. The fetal circulation and fetal hemoglobin protect the fetus against hypoxia. These compensatory mechanisms may be inadequate; however, when the pregnancy is already complicated by maternal anemia or placental insufficiency. Probably the greatest concern regarding high altitude travel in pregnancy, however, is that many high altitude destinations are remote from medical care.

Trauma

Trauma assumes greater importance during pregnancy, not only because it is more apt to occur, but also because it is more difficult to triage and treat. Loss of balance and lack of coordination increase the risk of falls. In addition, vascular dilation and ligamentous laxity increase the risk of injury to the woman. At the same time, emergency personnel tend to be very hesitant to undertake even routine investigations and procedures in the pregnant woman. In fact, treatment delay in pregnant women has been shown to increase the risk of fetal and maternal death [11].

Infectious Diseases

While the interactions of the environment and human pregnancy may be interesting, infectious diseases during pregnancy usually raise greater concern. We will briefly describe some of the effects of various diseases on pregnancy and vice versa.

Diseases with fecal-oral transmission

Traveler's diarrhea: Some illnesses are more common and more severe during pregnancy, requiring strict preventive measures and prompt treatment. An illustrative example is traveler's diarrhea. Decreased gastric acidity and slowed intestinal transit in pregnancy not only make diarrhea more likely but increase the risk of complications such as dehydration and ketosis [12]. Biochemical changes also mean that diarrhea will result more quickly in acidemia. The combination of this and dehydration may then lead to premature labor, hypovolemic shock and even fetal death [13].

Usually recommended are strict hygiene and food and water precautions, to be supplemented by vigorous oral hydration. Although they may become necessary, intravenous fluids should be avoided particularly in environments where sterile equipment cannot be guaranteed. Bismuth salicylate is contra indicated in pregnancy as the routine use of salicylates is not advised, and bismuth has been known to cause maternal encephalopathy and fetal hypotonus [14,15]. Antibiotics may be used when other measures are inadequate.

Hepatitis A and E: Hepatitis A infection is apt to have a fulminant course, fetal infection does occur and may result in fetal death [16]. Of greater concern is maternal infection with hepatitis E as very high maternal and infant mortality rates have been reported [17].

Brucellosis: Brucellosis is known to cause abortion and preterm delivery in domestic animals and to some degree in humans [18]. One

study reported up to a 43% miscarriage rate in the first two trimesters and a 2% fetal death rate in the third.

Listeria and toxoplasmosis: Two other infectious diseases that deserve special attention are listeriosis and toxoplasmosis [19,20]. Both of these infections are food-borne, most commonly in soft cheeses and raw or under cooked meats. Toxoplasma infection may also occur from handling soil in which cats have defecated. They are both more likely to occur in pregnancy and the illness more pronounced. The risk during pregnancy is that the infection will cross the placenta and cause spontaneous abortion, stillbirth, hydropsfetalis or congenital infection. Risk of fetal infection increases with length of gestation but severity of infection is decreased.

Typhoid and cholera: These are also infections that are often more severe in pregnancy, with a higher likelihood of death and, in the case of typhoid, hemorrhage from intestinal ulcers. Both may be passed transplacentally to the fetus. In the case of cholera, the risk of fetal death corresponds directly with the degree of maternal dehydration.

Amebiasis: Among parasitic diseases, only malaria and schistosomiasis result in more deaths than amebiasis. Children, especially neonates, pregnant women and women in the postpartum period have an increased risk for severe disease and death [21]. One study reported that two-thirds of the fatal cases of amebiasis occurred in pregnant women [22]. Vertical transmission of invasive disease may occur independent of maternal symptoms, causing clinical disease in the child either directly after birth or during the first months of life [23].

Giardiasis & cryptosporidia: These infections are neither more likely to occur nor to be worse during pregnancy but because of their chronicity may result in mal absorption, malnutrition and growth restriction of the fetus [24].

Echinococcosis & Cysticercosis: Echinococcal cysts are likely to grow more rapidly during pregnancy and have been reported to obstruct labor [25]. More commonly, these cysts will occur on or around the ovaries and may be inadvertently ruptured at surgery [26]. Neurocysticercosis becomes important during pregnancy when it causes seizures that are then mistaken for preeclampsia [27].

Helminths: In general, intestinal helminths rarely cause enough pathology to warrant treatment during pregnancy. Most intestinal helminths, in fact, can safely be addressed simply with symptomatic treatment until the pregnancy is over. Only severe cases, i.e. continued diarrhea leading to malnutrition require immediate therapy.

Water-borne disease

Schistosomiasis: Schistosomiasis is an important disease in women because it so frequently affects the reproductive organs and is a leading cause of infertility in many populations [28]. It has also been implicated in enhancing the spread of HIV and, when affecting the placenta, may contribute to fetal growth restriction or stillbirth [29].

Vector-borne diseases

Malaria: Malaria raises grave concerns for a number of reasons during pregnancy. Pregnant women appear to be more attractive to mosquitoes and therefore more at risk for malaria [30]. Also, pregnant women have an increased susceptibility to *P. falciparum* infection [31-35].

They are not only more apt to get malaria, the disease may be more difficult to diagnose due to sequestration of the parasites in the placenta. Malaria in pregnancy will often be characterized by very heavy parasitemia, severe anemia and sometimes profound hypoglycemia and may be complicated by cerebral malaria and pulmonary edema. Placental sequestration of parasites often results in fetal loss due to abruption, premature labor, and miscarriage. The infant born to the infected mother is more apt to be of low birth weight and to suffer from dehydration, seizures, thrombocytopenia and splenic rupture and although rare, congenital malaria is a concern [36-38].

Yellow fever: Congenital infection with yellow fever has been described, but overall the course of the disease appears to be unchanged in the pregnant versus the non-pregnant patient [39]. Most of the concerns regarding this disease are in regard to the administration of the vaccine during pregnancy. The predominance of evidence is that the vaccine is safe to use during pregnancy but may result in a lower titer of antibody response [40,41].

Trypanosomiasis: Pregnant women with chronic Trypanosomacruzi infection may present with cardiac or gastrointestinal symptoms and transmit the infection to their fetuses [42]. The infant may then develop the disease even some years later [43].

Dengue: Varying results have been shown in studies of dengue fever in pregnancy, but a review of these studies showed tendencies toward increased miscarriage, fetal death, dengue hemorrhagic fever and maternal death [44].

Leishmaniasis: Pregnancy seems to reactivate even latent visceral leishmaniasis and worsen its course with worse outcomes for both mother and child, and transplacental infection with both the cutaneous and visceral forms has been reported even many years after the primary infection [45-47].

Conclusion

As we have demonstrated in this brief review, the physiologic changes that occur with pregnancy may interact with the environment or with infections in such a way as to adversely affect the pregnancy or to worsen the course of the disease. These changes can also alter the body's response to vaccines or medications. For more detailed information readers are encouraged to read the articles referenced here and to take advantage of more complete information to be found in textbooks of infectious diseases and tropical and travel medicine.

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