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The Impact of Microorganisms in Pregnancy

Nastaran Ghandali[1], Hoda Sabati[2], Ali Emami[3] and Masumeh Dadashaliha[4*]

[1]Department of Biology, Faculty of Science, Shahid Chamran University, Ahvaz, Iran.
[2]Biotechnology and Biological Science Research Center, Faculty of Science Shahid Chamran University, Ahvaz, Iran.
[3]Qazvin University of Medical Sciences, Qazvin, Iran.
[4]Clinical Research Development Unit, Kosar Hospital, Qazvin University of Medical Sciences, Qazvin, Iran.

Authors' contributions

This work was carried out in collaboration among all authors. Author NG designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors HS and AE managed the analyses of the study. Author MD managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The pregnancy process involves many physiological changes, including weight gain, hormonal, metabolic and immune changes. One of the effective factors in this process is infection caused by microorganisms. Originally, before the advent of antibiotics, pregnancy was known as a risk factor for severe complications of pneumococcal pneumonia. Among viral infections, the 2009 flu pandemic issued a newer warning that some infections may disproportionately affect pregnant women and cause miscarriage and its complications during pregnancy. Generalization of pregnancy as a condition of suppression of the general immune system or increased risk is misleading and prevents the establishment of adequate guidelines for the treatment of pregnant women during epidemics. Viral infection has also become an important factor in pregnancy conditions. The recent outbreak of Ebola and other viral outbreaks and epidemics shows how pregnant women show worse outcomes (such as preterm delivery and fetal adverse outcomes) than the general population and non-pregnant women. The purpose of this article is studying pathogenesis of microorganisms and the risks which pose to the mother and the fetus. In order to investigate these factors, from 120 article prepared from google scholar and Pub med, Elsevier

**Corresponding author: E-mail: m.dadashaliha@qums.ac.ir;*

database. Knowing these factors can increase the ability to treat the infections in a timely manner and prevent their effects on the fetus and the patient.

Keywords: Pregnancy, virus, bacteria, fetus.

1. INTRODUCTION

Pregnancy is a dream of every couple, but infections during pregnancy associated with abortion and premature birth or fetal complications [1]. Pregnant women may be prone to infectious diseases. This subject reinforces the importance of infection prevention as well as early detection and treatment of infection during pregnancy [2]. Infections in pregnancy can be caused by a different mechanisms, including direct infection, placental damage, caused by various organisms, including many bacteria, viruses and protozoa [3]. Viral infections have been a major problem during pregnancy and can lead to worse outcomes (such as preterm delivery and adverse fetal outcomes) than the general population [4]. They also can have consequences for the fetus. Influenza, pertussis, Zika Virus and cytomegalovirus cause mild or asymptomatic illness in the mother but their major complications are for the fetus [5]. Ideally, a woman and her husband should consult with their General Practitioner when planning a pregnancy. Pre-pregnancy testing should include routine prenatal screening tests to prevent problems with delivery in pregnant women [6]. In this article, we investigate the infections caused by microorganisms in pregnancy.

2. MATERIALS

Due to the importance of pregnancy and the need to pay attention to it in medical sciences, this study was conducted in the form of review studies. This article contains 122 articles from Google Scholar, Pubmed and Elsevier database.

2.1 Bacteria

2.1.1 *Neisseria gonorrhea*

Neisseria gonorrhoeae (gonorrhea) is the second most prevalent STD in the United States. In Washington State in 2014, the incidence of gonorrhea infection in women ages 15–24 was 273 cases per 100,000 women and this has been rising in the past five year [7] Neisseria gonorrhoeae is A global STI surveillance in 2018 was conducted by the World Health Organization (WHO) and revealed an estimated 87 million new gonorrhoea infections globally during 2016, with an incidence of 20 cases per 1000 population in women . A study conducted exclusively on pregnant women reported a prevalence of 1.3% for N. gonorrhoeae [8] One of the most important reasons for infertility is tubular factor related to untreated sexually transmitted diseases that one of these causative agents is *Neisseria gonorrhea* [9]. *N.gonorrhea* is major causes of maternal and neonatal morbidity and mortality in developing countries [10]. This bacterium is one of the most important causes of pelvic inflammatory disease (PID) which in untreated women leads to infertility of the fallopian tube factor [11]. Chronic infections caused by this bacterium can cause urethral stricture and epididymo-orchitis in men [12]. This bacterium causes respiratory problems and infections in both sexes Gonorrhea also causes disseminated infection with complications that may result in ectopic pregnancy, tubal infertility, chronic pelvic pain or maternal transmission of gonorrhea and also increases susceptibility to human immunodeficiency virus (HIV) [13]. Women which infected with HIV-1 and HSV-2 were also at increased risk for *N. gonorrhea* and *chlamydia trachomatis*. Prophylactic screening and treatment of these common cervical infections, especially among people infected with HIV-1 and HSV-2, should be considered for young sexually active women [14]. Ceftriaxone is effective in treating gonorrhea in pregnant women. Amoxicillin is less effective and is not recommended for the treatment of gonococcal infections in pregnancy [15].

2.1.2 *Bordetella pertussis*

In the past 2 decades, the number of pertussis cases detected increased to ≈24.1 million/year; ≈161,000 deaths occurred during 2014 [16] Despite the advent of effective infant immunization programs throughout the world, pertussis, also called whooping cough, remains a significant cause of infant morbidity and mortality. The World Health Organization [17] numerous studies have evaluated the source of pertussis transmission to infants and typically report an unknown source of infection for ≥50% of infant cases.13–15 When a source is identified, mothers have been the most commonly cited source of infection in the United States (32%–37%) [18]. Pertussis is a preventable disease. Immunization of rubella to protect against pertussis depends on inactivated maternal

antibodies Antibodies received by the mother through the rubella vaccination series

However, pregnant women have very low concentrations of pertussis antibodies that must be passed on to the baby during delivery [19]. Immunization during pregnancy poses risks to the developing fetus. Although there is no evidence that the vaccine is harmful to the fetus but pregnant women should be careful about getting the vaccine [20]. It has been shown that maternal vaccine antibodies are normally transmitted through the placenta to the fetus [21].

2.1.3 Group B *Streptococcus* (GBS)

It is estimated that worldwide about 22 million women carry GBS with an estimated 410,000 infections in newborns every year, with at least 147,000 still births and infant deaths globally [22]. GBS infections in infants are restricted to very early infancy. Approximately 80% of infant infections occur in the first days of life, so-called early-onset disease [23]. *Streptococcus B* has been shown to be the leading cause of early complications for pregnant women and infant mortality in the United States [24]. Group B *streptococcus* (GBS) is a cause of sepsis in infants. Screening for this bacterium is recommended during prenatal care, because taking antibiotics can prevent the infection and complications caused by this bacterium in infants [25]. GBS is a major cause of perinatal infections during pregnancy [26]. Group B *streptococcus* remains the leading cause of neonatal sepsis and meningitis [27]. (Fig. 1).

2.1.4 *Listeria monocytogenes*

The incidence of listeriosis in pregnancy is 12 per 100,000, compared with a rate of 0. per 100,000 in the general population. The CDC monitors cases of listerial infection, and Cases were spread evenly throughout the United States. The incidence of listeriosis in the newborn is estimated at a rate of 8.6 per 100,000 live births [28]. *Listeria monocytogenes* is a bacterial pathogen that causes listeriosis, an important disease that lead to miscarriage in pregnant women [29]. Increased progesterone production during pregnancy reduces the function of the cellular immune system. As a result, many factors increase the risk of getting pregnant. One of these pathogens is *Listeria* [30]. Women who become infected with *L. monocytogenes* in the third trimester of pregnancy are usually treated with antimicrobials until the baby is born [31]. Tetracycline is contraindicated due to side effects and the ability of the crossing placenta [32] The use of quinolone in the first trimester of pregnancy also had risks including major birth defects, preterm birth or low birth weight [33].

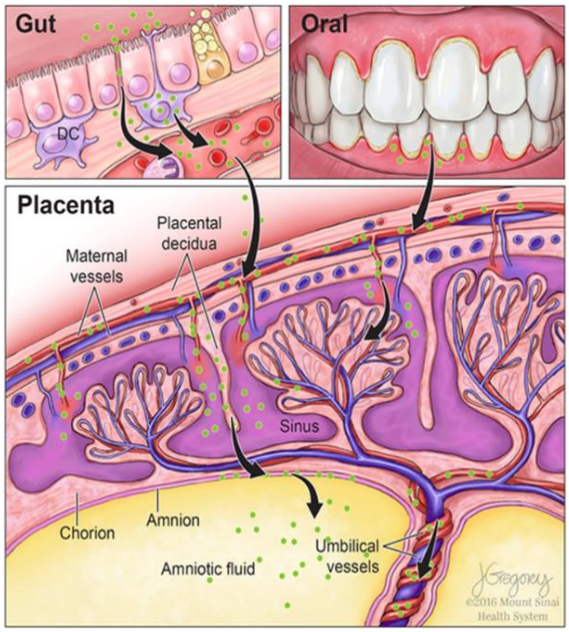

Fig. 1. Proposed mechanisms of maternal transfer of bacteria to the fetus in utero [153]

2.1.5 *Mycobacterium tuberculosis*

Worldwide, the burden of tuberculosis (TB) disease in pregnant patients is substantial. It was estimated that more than 200,000 cases of active TB occurred among pregnant patients globally in 2011; In the United States between 2003 and 2011, the incidence of TB in pregnancy was 26.6 per 100,000 births [34]. Tuberculosis (TB) caused by this bacterium is very important and of course is less noticeable. Treatment of tuberculosis in pregnancy and the potential dangers of its drugs on the pregnancy process are significant [35]. To diagnose this disease in pregnant women, especially women with tuberculosis, morning sputum samples were taken [36]. In terms of immunity, T cells and T cell-derived cytokines are essential mediators of protection against mycobacterium tuberculosis infection [37]. Gynecologists in a unique situation recommend identifying people with TB: medical history, abnormal physical examination and positive laboratory tests. If a pregnant woman has signs or symptoms of tuberculosis, she should be treated before giving birth [38].

2.1.6 *Treponema pallidum*

CDC reported that the rates of both female increased during 2005–2008 in the United States of America (USA), and have since declined. The rate of syphilis among women was 1.1 cases per 100,000 women in 2010 [39]. Congenital syphilis is still a major cause of perinatal disease and mortality. Untreated maternal infection can cause problems such as premature fetal loss, stillbirth, prematurity and low birth weight in infants [39]. Proper treatment of pregnant women often prevents these complications. First trimester screening is non-treponemal tests for syphilis such as plasma retest (RPR) or venereal disease research laboratory test (VDRL) [40].

2.1.7 *Mycoplasma genitalium*

M. hominis is the first bacterium of human origin isolated in 1973. This bacterium is found in the vagina of 2.3% of women with bacterial vaginosis and 10% of healthy women [41]. The prevalence of M. genitalium was 0.7%. It was more common in women aged < 20 years, women of Afro-Caribbean or black African ethnic origin, women in social classes 3-5 and single women [42]. *M. genitalium* is a sexually transmitted disease that cause urethritis. Inflammatory genitals are involved in women including cervicitis, pelvic inflammatory disease and infertility [43]. *M.genitalium* is an important pathogen in the infection control protocols [44]. Macrolides, especially single-dose azithromycin are recommended for the treatment of genital Infection caused by *M.genitalium* [45].

2.1.8 *Chlamydia trachomatis*

Chlamydia is a sexually transmitted disease of epidemic proportions, infecting an estimated 4 million people a year. Ectopic pregnancy is responsible for 11 percent of maternal deaths. [46] About 60 percent of infected women can transmit the bacteria at birthIn the Netherlands, a chlamydial prevalence of 2.5% was reported in women . However, prenatal screening for C. trachomatis is not routine obstetrical practice in the women [47]. *Chlamydia trachomatis* is the most common sexually transmitted bacterial infection. Symptoms include vaginal discharge, subsequent bleeding and menstrual bleeding. This can cause problems such as urethritis, cervix, adnexa, pelvic inflammatory disease or ectopic pregnancy [48]. The bacteria is transmitted to the baby during delivery. Neonatal infection may develop as conjunctivitis and pneumonia [49].

2.2 Viruses

2.2.1 *Human Immunodeficiency Virus*

According to one estimate, around 5,000 HIV positive women give birth in the United States every year. . In the United States, black infants have 5 times increased incidence of perinatal HIV compared to white infants. According to a report by the Centers for Disease Control and Prevention, only 44 HIV positive infants were born in the United States in the year 2016, with the incidence of perinatal HIV transmission being as low as 1.1 out of 100,000 live births [50]. Worldwide, approximately 35 million people are infected with HIV and almost half of them are women [51]. The number of pregnant women living with HIV is increasing every year [52]. Little is known about how HIV is diagnosed and cared for during women's reproductive years [53]. HIV-infected women are likely to have prolonged ovulation and the underlying mechanisms are unknown [54]. HIV infection may affect fetal immunity and susceptibility to postpartum infections [55]. Given the significant advances in preventing HIV perinatal transmission, it is clear that early diagnosis and treatment of pregnant women with this disease is the best way to prevent neonatal infections [56]. Diagnostic tests

should be done before the baby is born. These tests should also be done after the baby is born because the mother may become infected during pregnancy or childbirth [57]. In the treatment of this disease in pregnant women, the use of multiple antiretroviral drugs during pregnancy reduces the rate of HIV transmission in pregnancy but concerns about the side effects of these drugs on the fetus are under investigation [58].

2.2.2 *Corona virus*

During January 22–June 7, among 1,573,211 laboratory-confirmed cases of SARS-CoV-2 infection reported to CDC as part of national COVID-19 surveillance, a total of 326,335 (20.7%) occurred among women aged 15–44 years. Data on pregnancy status were available for 91,412 (28.0%) of these women; 8,207 (9.0%) were pregnant [59]. A new epidemic of the corona family is underway. Previous epidemics often result in poor delivery outcomes including maternal mortality, maternal and fetal virus transmission and gynecological infections. There is no evidence that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted through uterine transmission to the infant [60]. The risk of pregnancy complications such as preeclampsia and premature birth is more common in pregnant women. Angiotensin-converting enzyme 2 (ACE2) and its expression increase during pregnancy which may provide favorable conditions for SARS-CoV2 infection. Coronavirus disease 19 (Covid-19) may eventually lead to premature preeclampsia and worsening maternal disease [61]. Guidelines for delivery and care of infants during pregnancy should be provided with COVID-19 due to the potential for vertical transmission, which recommend routine separation of infected mothers and their postpartum infants [62]. The virus can also increase the risk of pregnancy complications, so the pregnant mother should be admitted to a health care center and given birth under the supervision of gynecologist [63].

2.2.3 *Rubella virus*

Congenital rubella infection (CRI) has outcomes including miscarriage, stillbirth, abortion, congenital rubella syndrome (CRS) or asymptomatic infection in the infant. The risk of congenital defects varies from 10% to 90% depending on the gestational age of the fetus at the time of infection. The occurrence of rubella earlier in gestation, particularly during the first 12 weeks, increases the risk of more severe. Africa and South East Asia regions, with the respective estimated incidence of 116 and 211 per 1 00 000 live births in 2010, have the highest rates of CRS. In Ethiopia, estimates of the rate of CRS range from 24 to 112 per 1 00 000 live births in urban Addis Ababa and rural Ethiopia, respectively [64]. TORCH infections include: Toxoplasmosis, *Treponema pallidum*, rubella, cytomegalovirus, herpes, hepatitis viruses, human immunodeficiency virus and other infections such as varicella, parvovirus B19, enteroviruses and measles that is caused by rubella viruses [65]. However, due to vaccination, the possibility of transmitting the virus is rare. In some countries, congenital rubella syndrome (CRS) is one of the leading causes of growth abnormalities, especially blindness and deafness [66]. prevent problems with rubella, screening and vaccination of susceptible women is important to reduce the risk of congenital rubella syndrome [67].

2.2.4 *Herpes simplex virus (HSV)*

pregnant women, the seroprevalence varies from 7.6% to 8.4%. in US, approximately 22% of pregnant women are infected with HSV-2, and 2% of women acquire genital herpes during pregnancy [68]. Hepatitis HSV is a rare disease that commonly affects immunocompromised patients, including pregnant women [69]. Neonatal HSV infection during pregnancy is a rare but can be associated with high mortality rate [70]. Pregnant women are also more likely to infect HSV which causes hepatitis. Diagnosis of HSV hepatitis and starting appropriate treatment with acyclovir at 36 weeks of gestation reduces the risk of pregnancy [71]. Acyclovir is effective in treating the disease but does not significantly reduce viral lesions in late pregnancy [72].

2.2.5 Varicella zoster virus (VZV)

Best estimates suggest an incidence of 2–3/1000 in the UK5 and between 1.6 and 4.6/1000 in the USA among 15–44 year old individuals during the 1990 [73]. Varicella zoster virus (VZV) is an alpha herpes virus that causes varicella (chickenpox) and herpes zoster (shingles) [74]. Infection with the virus is associated with serious fetal and maternal complications. Vaccination against varicella zoster virus can prevent the disease [73]. It has also been shown the rapid treatment of the disease with Acyclovir, significantly improve the symptoms in the patients [75].

2.2.6 *Hepatitis E virus (HEV)*

Hepatitis E virus (HEV) is a leading cause of acute viral hepatitis globally [78]. There are an estimated 20 million HEV infections, 3.3 million symptomatic hepatitis E cases, and 60,000 deaths worldwide[76] In men and non-pregnant women, the disease is usually self-limited and has a case-fatality rate of less than <0.1% [79]. the seroprevalence of HEV infection among pregnant women is between 3.6% and 7.4% (77). *Hepatitis E virus (HEV*) is an uncovered RNA virus that is responsible for major hepatitis epidemics which is the important of for liver failure [78]. Viral hepatitis in the pregnant women with HEV infection associated with delivery complications such as intrauterine fetal death and poor outcomes for the fetus [79]. Acute liver failure also occurs in a large number of pregnant women, mostly in the third trimester [80]. During pregnancy, the levels of progesterone, estrogen and gonadotropin in the placenta increase. These hormones play an important role in altering the immune system and predispose them to infection [81].

2.2.7 Hepatitis C virus (HCV)

According to the U.S. Centers for Disease Control and Prevention, an estimated 23,000 to 46,000 children in the United States live with HCV infection. Notably, children born to HCV-positive mothers are at particular risk of HCV infection. Africa is hyperendemic with respect to viral hepatitis B and C infections, with a prevalence of detectable HCV viral load of 62.3% in HCV-positive pregnant women. Infected mothers have a high potential for transmission to their children [82]. The rate of pregnant women potentially infected with HCV was twice as lower than that in a control group of women undergoing tests for other medical circumstances: 0.76% vs 1.67% ($P < 0.0001$) [83]. HCV-positive pregnant women appear to be at risk for adverse outcomes for infants and mothers. No intervention has been clearly demonstrated to reduce the risk of mother-to-child transmission of HCV. It does not clear that breastfeeding should be avoided to reduce the risk of transmission [84]. Hepatitis C virus can be transmitted to the baby during pregnancy and infection during pregnancy increases the risk of fetal side effects including fetal growth retardation and low birth weight [85]. Also, newborns with chronic hepatitis C are more likely to be underweight and need assisted ventilation or neonatal intensive care units (NICU) [86].

2.2.8 *Hepatitis B virus (HBV)*

Hepatitis B virus (HBV) infection is a global public health problem. The WHO estimates that more than 2 billion people have been infected with HBV [87]. The incidence rate of pregnant women in a study in Nigeria was estimated at 8.2 [88]. Maternal-to-child perinatal transmission (MTCT) of hepatitis B virus (HBV) is the most important risk factor for chronic HBV infection in neonates. In addition to hepatitis B immunoglobulin, immunization and vaccination can reduce MTCT [89]. Caesarean section before delivery or before ruptured membrane (elective caesarean section) has been introduced as an intervention to prevent mother-to-child transmission of disease. There is currently no evidence that caesarean section reduces MTCT versus vaginal delivery [90]. Its effectiveness and safety in mothers in reducing hepatitis B virus from mother to baby is not clearly understood. HBV is a risk factor for preterm delivery and maternal infectious complications such as late miscarriage [91]. HBV is a risk factor for preterm delivery. Bacterial vaginosis (BV) is a complication of pregnancy in which vaginal infections are common in the third trimester of pregnancy [92]. Valuable viral recurrence occurred after cessation of treatment and in pregnancy, the infected mother affects the immune system of the fetus (Fig. 2).

2.2.9 *ZIKA Virus*

In previous studies in the United States, infection in the first trimester was associated with congenital birth defects in 11% of women with evidence of ZIKV infection [93]. Zika virus is a mosquito-borne virus that was first identified in Uganda in 1947 [94]. Zika virus is primarily transmitted to humans through the bite of Aedes mosquitoes which is associated with an increase the risk of microcephaly [95]. (Fig. 3). ZIKV infection during pregnancy leads to catastrophic consequences of neurodevelopment in the human fetus but there is currently no effective treatment or prevention of ZIKV infection other than avoiding mosquito vectors [96]. A diagnostic test for Zika virus is the IgM antibody which can persist for more than 12 weeks after infection. Therefore, it does not report the results very accurately [97].

2.2.10 *Cytomegalovirus (CMV)*

CMV is the most common virus passed from mothers to babies during pregnancy. About 1 to 4 in 100 women (1 to 4 percent) have CMV

during pregnancy [98]. Each year, a number of pregnant women develop primary CMV infection. The risk of serious fetal complications is higher when the infection occurs in the first trimester or early of the second trimester [99]. If you have CMV during pregnancy, you have a 1-in-3 chance (33 percent) of passing it to your baby. CMV is the most common virus passed from mothers to babies during pregnancy. About 1 to 4 in 100 women (1 to 4 percent) have CMV during pregnancy [98]. Primary CMV infection is a major problem in pregnancy and due to the lack of safety treatment, routine prenatal screening for CMV should be performed for women [100]. In pregnant women with CMV, the CD_8 T cells of pregnant women are transferred to the fetus which indicates the presence of the virus in the placenta [101]. Treatment of congenital symptomatic cytomegalovirus is intravenous ganciclovir for 6 weeks that showed the improvement in hearing loss [102]. Oral therapy with oral valganciclovir is helpful in a very low birth weight preterm infant with CMV infection [103]. Fetus with congenital CMV infection during first trimester are more likely to have CNS sequelae, especially sensorineural hearing loss [104].

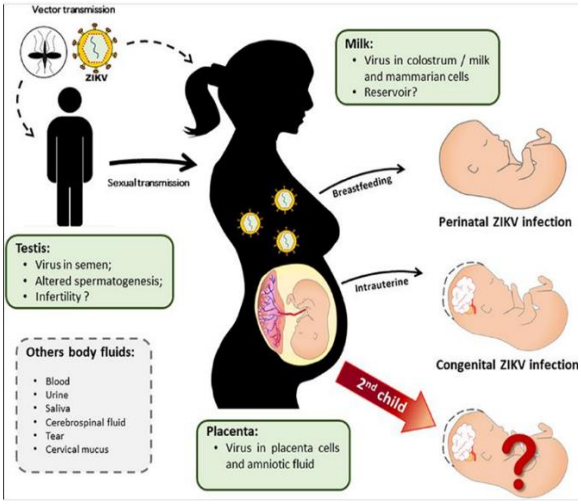

Fig. 2. Schematic representation of immunologic changes in the peripartum period in mothers with chronic hepatitis B [154]

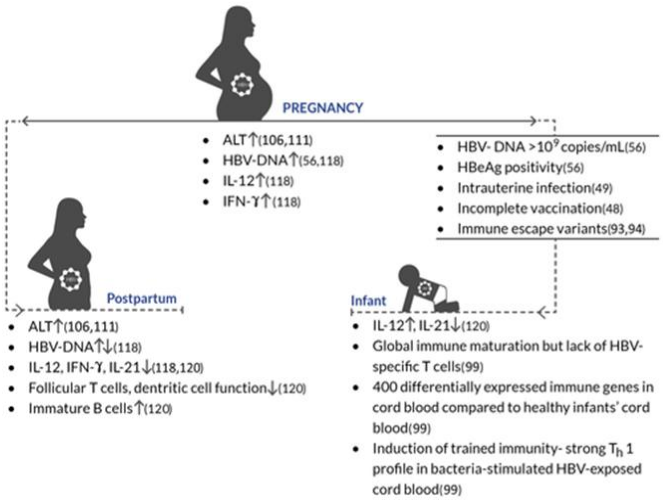

Fig. 3. ZIKV vertical transmission. This transmission may occur in pregnant women through mosquito bites or sexual contact with an infected partner. Mother-to-child transmission can also occur in the uterus [155]

2.2.11 *Influenza*

Although appreciated for centuries, the impact of pandemic influenza on pregnant women and their unborn children was first examined systematically during the 1889, and more substantially during the 1918 pandemics, killed 675 000 persons in the United States, with an overall case fatality rate of 1–2%. Numerous studies indicated that pregnant women were at greatly elevated risk of severe disease and death [105].

Pregnant women are at risk of influenza. However, the flu has been shown to affect the cardiovascular and pulmonary systems during pregnancy [106]. The 2009 flu pandemic offers a newer view that some infections may disproportionately affect pregnant women [107]. It has also been shown that if the virus causes a viral infection of the placenta, the placental virus may make the pregnant mother susceptible to bacterial products and cause preterm labor [108]. If you are vaccinated to prevent the flu virus, injecting a certain amount will create an adequate level of immunity in the immune system [109]. Influenza infection is also more severe in the second and third trimesters of pregnancy and leads to more complications and mortality [110]. Immunization of the mother is especially important in considering vaccine-preventable diseases such as influenza [111]. In the case of neonatal vaccination, it is noteworthy that the stable high levels of anti-influenza IgA that are actively produced in breast milk indicate that breastfeeding may protect the baby for some time [112]. Affected pregnant mothers should receive antiviral treatment for 5 days. Oseltamivir is the preferred treatment for the pregnant women [113].

2.2.12 Parvovirus B19

Parvovirus B19 is a widespread infection that may affects 1-5% of pregnant women, mainly with normal pregnancy outcome. The prevalence of infection is higher during epidemics - between 3 and 20% with seroconversion rate of 3-34%. Infection during pregnancy can cause a variety of other signs of fetal damage [114]. Maternal infection in the first half of pregnancy is associated with fetal death and hydrops fetalis [115]. Parvovirus B19 infection can infect the fetus and in rare cases causes brain abnormalities and nerve damage [116]. Fetal parvovirus infection can lead to anemia in formation of the hydrops fetalis. There is no vaccine for this virus [117]. B19 infection is often asymptomatic or mild in the general population but may be transmitted from mother to fetus during pregnancy [118].

2.2.13 Human Papillomavirus

The prevalence of genital Human papillomavirus (HPV) infection during pregnancy is high (about 40%) [119]. reported the prevalence of HPV infection in pregnant women with a wide variation from 5.5 to 65% (120). HPV is the most common sexually transmitted infection in the world [121]. HPV infection may be triggered by hormones [122].

2.3 Parasites

2.3.1 Trichomonas vaginalis

Trichomoniasis is the most prevalent non-viral sexually transmitted disease (STD) in the world, with an annual incidence of 276.4 million cases. Studies in Latin America show that the prevalence of trichomoniasis is approximately 3.9%, which is higher than the prevalence of Neisseria gonorrhoeae (1.2%) and syphilis (1.1%). Among pregnant women in Brazil, studies have recorded a prevalence of 7.7% [123]. *Trichomonas vaginalis* is a sexually transmitted disease (STD), mainly in women who are asymptomatic or can cause vaginitis, cervicitis, urethritis and pelvic inflammatory disease (PID) [124]. Infection with *trichomonas vaginalis* during pregnancy may also be associated with preterm delivery. It has also been shown that treating asymptomatic pregnant women does not prevent preterm delivery [125]. *T. Vaginalis* has only a small effect on male fertility [126].

2.3.2 Plasmodium falciparum

Plasmodium falciparum is one of the leading causes of malaria. According to the estimated annual report, the number of pregnant women who were at risk of malaria was about 25 million. It has been reported that in sub-Saharan Africa malaria can cause as many as 10,000 cases of malaria-related deaths in pregnancy per year, usually due to severe maternal anemia [127]. Women are especially susceptible to malaria during the first and second trimester, even they become immune during years of living in the native area [128]. *Plasmodium* has serious side effects such as miscarriage, low birth weight and anemia [129]. Decreased activity of natural killer

cells, inflammatory macrophages and T helper 1 (Th1) cells along with increased activity of T regulatory cells and production of anti-inflammatory cytokines, affect the pathogenesis of the disease [130]. Increased use of preventive protocols for malaria is the important opportunity to improve birth outcomes and infant health care [131]. The treatment is folic acid supplementation in high doses and detrimental anti-inflammatory effects of anti-malarial drugs such as sulfadoxine / pyrimethamine [132].

2.3.3 Plasmodium vivax

In Latin America, where malaria transmission is low and mostly unstable, Plasmodium vivax is the most prevalent malaria parasite species. Although ≈3 million pregnant women are exposed to malaria in Latin America each year, the actual number of malaria infections during pregnancy is considerably lower [133]. Through the mid-20th century, malaria was endemic in much of the United States, with approximately 300 cases per 100,000 population in 1920 [134]. Most pregnant women who are at risk for *plasmodium vivax* infection, live in Asia-Pacific [135]. *Plasmodium vivax* infections are rarely killed directly but can cause indirect death by low birth weight at birth [136]. Although *P. vivax* infections are clearly associated with serious adverse outcomes during pregnancy, accumulation of *P. vivax* in the placenta has not been reported. Approximately half of *P. vivax* infections are asymptomatic, which early strategies related to malaria prevention is necessary [133].

2.3.4 Toxoplasma gondii

While infection in early pregnancy poses a small risk of fetal transmission (less than 6%), rates of transmission range between 60% and 81% in the third trimester [137]. Toxoplasmosis can be a severe systemic congenital disease [138]. *Toxoplasma* can be passed from mother to fetus, so it may cause complications for fetus, intrauterine abortion and fetal death [139].

2.4 Fungus

2.4.1 Candida

Candida is the leading cause of vaginitis, and 75% of women have at least one episode of infection in their lives, with pregnancy being a predisposing factor [140]. Because of the increased production of sex hormones, vaginal candidiasis is common during pregnancy, affecting up to 10% of pregnant women in the United States [141]. *Candida albicans* causes candida vaginitis occurs worldwide [142]. *Candida albicans* accounts for 80-95% of all Candida vaginitis cases in worldwide [143]. Pregnant women are at risk for vaginal candidiasis due to increased secretion of sex hormones. Prevalence of vaginal candidiasis in pregnant women in the United States is estimated at 10% [144]. Candida infection is also a major cause of volvo-vaginitis [145]. Amphotericin B is the most sensitive antifungal drug. High rates of multiple drug-resistant in candida species were observed. Therefore, symptomatic women should be screened and treated regular [146]. Pregnancy increases the rate of vaginal candidiasis in women, especially in the third trimester of pregnancy. One of the effective ingredients is tea tree oil (TTO) which causes cell death by destroying the structure of the cell membrane and changing its permeability [147]. It is suggested that early treatment of candida vaginal infection during pregnancy can greatly reduce the rate of fungal infections in the fetus [148].

2.4.2 Coccidioides

The incidence of coccidioidal infections in Arizona, Nevada, California, New Mexico, and Utah has increased from 5.3 per 100,000 in 1988 to 42.6 per 100,000 in 2011. Around 75,000 deaths per year result from the infection. This increase in the disease occurrence requires particular attention in the pregnant population, since the consequences could manifest not only in the dissemination of coccidioidomycosis, but also result in fetal disease, congenital anomalies and other developmental sequels [149]. Pregnancy is a risk factor for severe and widespread coccidioidomycosis [150]. Coccidioidomacosis during pregnancy is a devastating disease that is associated with high maternal mortality. Women who develop coccidioidomycosis in late pregnancy are at risk for severe infection [151]. It has also been shown that the main effect at the beginning of the first trimester of pregnancy is the tendency to have an abortion. In cases starting from the third trimester, the prevalence of preterm delivery was high [152].

3. CONCLUSION

In this review, we talk about microbial infection during pregnancy. Basically one of the important factors in pregnancy is the disease caused by microorganisms including bacteria, virus, fungi

and parasite which a high percentage of complications in the fetus are caused by these factors. Potential infections have been shown to cause miscarriage and may be transmitted from mother to fetus, that cause complications in the fetus. It is important to screen these diseases and treat their infections to improve fertility outcomes. Bacterial and viral infections have been shown to have a greater effect on abortion and fetal complications than fungal and parasitic infections.

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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