

INFECTIONS CAUSED BY TORCH PATHOGENS CLASSIFIED AS "OTHER"

ZAKAŻENIA POWODOWANE PRZEZ PATOGENY GRUPY TORCH OKREŚLANE JAKO „OTHER”

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dane – analiza i statystyki
D. Data interpretation
interpretacja danych
E. Preparation of manuscript
przygotowanie artykułu
F. Literature analysis/search
wyszukiwanie i analiza literatury
G. Funds collection
zebranie funduszy

Tables: 0
Figures: 0
References: 44
Submitted: 20.10.2015
Accepted: 21.01.2016

Summary

The aim of this study was to present the characteristics of infections caused by the TORCH complex pathogens, identified as "others", in women during pregnancy and their influence on the foetus.

The "other" TORCH pathogens include: *Treponema pallium*, *Listeria monocytogenes*, Parvovirus B19, Varicella zoster virus, Measles virus, Myxovirusparotitis, influenza virus, viruses such as: HIV, HCV, HBC and also *Chlamydia trachomatis*. These pathogens are not only responsible for developing certain clinical symptoms in pregnant women but they also have a significant influence on child's health and might be the cause of congenital disorders in infants. The consequences of TORCH infections may be visible in children directly after the birth, during infancy, or become present later, after several years. The most serious consequences are caused by foetal infection during early pregnancy. They may result in severe congenital disorders in foetus or cause miscarriage. Tests and examinations of women who plan pregnancy, and regular checks of the course of pregnancy allow for a proper care of mother and child.

Keywords: TORCH, pregnancy, foetus, infections, vaccinations, prophylaxis

Streszczenie

Celem pracy było przedstawienie charakterystyki zakażeń powodowanych przez patogeny kompleksu TORCH określane jako „others” u kobiet w okresie ciąży z uwzględnieniem ich wpływu na płód.

Do patogenów „others” panelu TORCH należą: *Treponema pallium*, *Listeria monocytogenes*, Parvovirus B19, Varicella zoster virus, Measles virus, Myxovirusparotitis, wirus grypy oraz wirusy HIV, HCV, HBV jak również *Chlamydia trachomatis*. Patogeny te odpowiedzialne są za generowanie określonych objawów klinicznych u ciężarnej lecz mają również istotny wpływ na zdrowie dziecka i mogą być przyczyną wad wrodzonych u noworodków. Skutki zakażenia drobnoustrojami z grupy TORCH mogą być widoczne u dzieci bezpośrednio po urodzeniu, w okresie niemowlęcym lub ujawniać się w latach późniejszych. Do najpoważniejszych konsekwencji prowadzą zakażenia płodu we wczesnym okresie ciąży. Mogą one nieść ze sobą ciężkie wady rozwojowe płodu lub powodować utratę ciąży. Badania kobiet planujących macierzyństwo i okresowe kontrole prawidłowości przebiegającej ciąży pozwalają na właściwą opiekę nad matką i dzieckiem.

Słowa kluczowe: TORCH, ciąża, płód, zakażenia, szczepienia, profilaktyka

Introduction

TORCH complex pathogens include: *Toxoplasma gondii*, *Rubella virus*, *Cytomegalovirus*, *Herpes simplex virus*. "Others" are, as follows: *Treponema pallium*, *Listeria monocytogenes*, Parvovirus B19, *Varicella zoster virus*, *Measles virus*, *Myxovirusparotitis*, influenza virus, viruses such as: HIV, HCV, HBC and also *Chlamydia trachomatis*, and *Plasmodium falciparum* [1, 2]. These pathogens are not only responsible for developing certain clinical symptoms in pregnant women but also have significant influence on child's health. The consequences of TORCH infections may lead to foetal death, development of congenital disorders or damages which may be visible in children directly after the birth, during infancy, or become present later, after several years. The most serious consequences are caused by foetal infection during early pregnancy [1,2].

Treponema pallidum - syphilis etiological factor

Syphilis is a systemic infectious disease caused by spirochete bacterium *Treponema pallium* the primary route of transmission of which is through sexual contact. Every year, 12 million new infections are registered worldwide, mainly in developing countries, which may be a result of the change in life style and risky sexual behaviours [3]. According to the National Institute of Public Health [4] 18 cases of congenital syphilis were

Fiedoruk M, Laskowski K, Tokarska-Rodak M. Infections caused by TORCH pathogens classified as "other". Health Problems of Civilization 2016; 10(2): 55-63. doi:10.5114/hpc.2016.59634.

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registered in 2013, in Poland (prevalence: 4.87 per 100 000), whilst the general number of cases amounted to 1258 (prevalence: 3.27 per 100 000). Preliminary data from 2014 suggests the increase in number of congenital syphilis infections to 20 (prevalence: 5.41 per 100 000) while the general number of cases amounts to 1233 [5].

Congenital syphilis develops as a result of intrauterine foetal infection with *T. pallidum* spirochete. The infection may occur already during early pregnancy between the 6th and the 10th week, however, most frequently it is transferred after the 20th week via placenta route. The high risk of infection occurs also during the childbirth, whilst the exacerbation of foetal infection depends on the mother's stage of the disease. The highest level of risk of foetal infection and its severe damage occurs when the mother's disease is at early stage: 70-100%, in case of primary latent syphilis: 40% and in case of secondary infection: 10% [3].

Congenital syphilis infection is a mother-to-child transmission of the disease that occurs during pregnancy or childbirth. Degree of disease advancement might have a dual nature - from a labour on the due date without any signs of infection to the miscarriage or death of a child straight after the childbirth [6].

Congenital syphilis may be classified as: early, that occurs in up to 3-year old children and late, in which symptoms are manifested in children at 3 years of age or older. Typical symptoms and signs of congenital syphilis include: "old-man appearance", skin lesions, abnormal mucous membrane, abnormalities in body organs, development disorders, skeletal abnormalities, breathing difficulties. Skin lesions are characterised by: flat rash on the face, palms and feet, and bumpy rash merging on the buttocks, palms and feet into copper-coloured lesions, so-called: "coloured buttocks" [7]. Most frequently, congenital syphilis course is asymptomatic and symptoms may occur only between 8 and 14 years of age. 20% of all infections are manifested by the inflammation of the front of the eye (the cornea) that leads to blindness; abnormal notched and peg-shaped teeth, called Hutchinson teeth; parrot scars around the mouth and anus. In children with this infection decrease of hearing or even deafness may occur caused by vestibulocochlear nerve damage; they may also suffer from intellectual disability [3].

The diagnosis is based on clinical symptoms, signs'occurrence, and methods of laboratory diagnostics. Diagnostics consists of non-specific serological testing: Venereal Disease Research Laboratory (VDRL) test, the unheated serum reagin (USR) test that detect bacteria antiphospholipid antibodies, and specific testing: the fluorescent treponemal antibody absorption (FTA-Abs) test, treponema pallidum hemagglutination assay (TPHA) that detect antibacterial antibodies. Smear tests sampled from skin lesions and molecular diagnostic methods (PCR) may also be efficient.

In its recommendations about antenatal care during pregnancy in case of regular course, the Polish Gynaecology Society suggests to perform VDRL tests, repeated twice - in 7-8th week and 33-37th week [8].

***Listeria monocytogenes* - etiological factor of listeriosis**

Listeriosis is a bacterial infectious disease that occurs in humans and animals and is caused by *Listeria monocytogenes* bacillus. These bacteria are one of the significant etiological factors that cause dangerous infections of the central nervous system, sepsis, and also infections in pregnant women. Infection with *L. monocytogenes* may lead to miscarriage, stillbirth or congenital listeriosis which may be the cause of death in about 50% of infants [9]. The bacteria live in natural environment and most of the infections are related to consumption of processed food mainly meat products as well as contaminated dairy products, fruits and vegetables [10,9]. The main route of acquisition of *Listeria* is through the ingestion of contaminated food products, however, the infection may also occur after direct exposure to pathogens by intact skin and sexual contacts with an infected person. Vertically transmitted infections include: transplacental infection and perinatal infection that is related to presence of pathogens in the mother's genital tract [7]. 27% of all *L. monocytogenes* infections concern pregnant women, most frequently those in the third trimester which stands for 1/3 of all diagnosed cases. The course of the disease in case of a mother is usually mild. At the first stage of infection it is manifested by symptoms that resemble influenza, such as: high fever (38-41°C), headaches, sore throat, diarrhoea or pyelonephritis [11,10]. As the infection spreads through placenta into amniotic fluid and amniotic sac it causes intrauterine foetal infections and, in result, leads to foetal death, miscarriage or preterm birth. In 60% of infants whose mothers suffered from the disease during pregnancy there is an onset of full-blown disease [11]. Early-stage listeriosis is diagnosed when the symptoms occur in the first week of infant's life and are related to prolonged intrauterine infection. This form may be accompanied by: sepsis, pneumonia, acute respiratory failure, CNS infection, characteristic skin lesions that appear most often on the back and buttocks, conjunctivitis, rhinitis, liver and spleen enlargement [3, 7]. Late-stage is diagnosed when symptoms become manifested later than 7 days after the birth and occurs in infants infected shortly before the birth or during the birth. The most characteristic symptoms of the late stage are sepsis, and also meningitis that develops in 90% of infected infants [3].

The diagnostics of *L. monocytogenes* infection in mother is based on blood culture in case of fever of unknown origin and also on cervical smear sampling. In infants, cerebrospinal fluid and blood tests are conducted, and also meconium, urine and gastric content are microbiologically tested. The polymerase chain reaction (PCR) methods and serological tests based on assessment of the listeria antibodies concentration are used to recognize *L. monocytogenes* [10].

The prevention is based on education for pregnant women about excluding certain foods from diet that may potentially be infected with *L. monocytogenes*, such as: soft cheese (Brie, Camambert) and pâté (cooked ground meat and fat minced into a spreadable paste) [7].

***Chlamydia trachomatis* infections**

Chlamydia trachomatis is one of the main etiological factors of sexually transmitted bacterial infections. Serovars D-K, also called oculogenital serovars, cause urethritis in adults and perinatal infections in infants [12]. Depending on a population, several to 40% of people suffer from *C. trachomatis* infection [13]. It is estimated that the percentage of *C. trachomatis*-infected women amounts to 20-30% and has shown an increasing tendency for last few years. Risk factors are, as follows: age less than 25 years, early sexual initiation, a large number of sexual partners, use of oral contraceptives and non-barrier contraceptive methods, infections with other sexually transmitted diseases, pathology of the cervix, pregnancy [3].

The course of early stages of *C. trachomatis* in 50% of cases is asymptomatic. In women with infection in cervix, genitourinary system, urethra, the lining of the anus non-specific symptoms are observed: purulent secretion from the cervical canal, contact bleeding from the cervix or dysuria [3]. Chronic inflammation of cervix related to *C. trachomatis* infection is connected to the possibility of the formation of a neoplastic changes [12]. Bartholin gland and appendages inflammation and endometritis, and menstrual cycle disorders may occur in advanced stage of infection. Recurring *C. trachomatis* infections may be related to the risk of ectopic pregnancy, infertility and myocarditis, and joints inflammation [3].

In pregnant women the *C. trachomatis* infection may be the cause of disorders that lead to pathological course of pregnancy, miscarriages, preterm birth, perinatal infections and, in early stages of pregnancy, increase the risk of miscarriage or intrauterine foetal death [12,3].

Neonatal infection occurs while the foetus passes through the birth canal however, cases of infection during caesarean section have also been noted. In this case, acquisition is due to the earlier amniotic fluid infection [12]. *Chlamydia trachomatis* may cause: conjunctivitis in infants (50%), pneumonia that develops 2 weeks after the birth (up to 15%) and, rarely - meningitis, otitis media, carditis [3]. Conjunctivitis may differ in intensification - from asymptomatic infection to acute, purulent conjunctivitis whose course may lead to complications: papillary hyperplasia within the upper eyelid, conjunctival scarring, cornea vacuolation.

The diagnostics of *C. trachomatis* infection include sampling of: urine, swabs of the cervical canal, urethra, conjunctivitis, anus, throat. In pregnant women in whose there is a leakage of amniotic fluid it also can be sampled. In case of perinatal infections in children, tears, conjunctival swabs, bronchial lavage are sampled [12].

In *C. trachomatis* infections diagnostics flowing methods are used: direct microscopic examination detecting inclusion bodies, antigen detection test by the direct immunofluorescence or by enzyme-linked immunosorbent assay (ELISA), McCoy or HeLa 229 cells cultures, the determination of anti-*C. trachomatis* in serum and molecular studies [13].

Early diagnostics and elimination of the mother's infection allows for the reduction of the risk for contact between pathogen and the foetus during pregnancy thus, allows for decreasing the risk of preterm birth [14].

Human immunodeficiency virus (HIV) infection

According to estimated WHO data from 2014, 67% of HIV-positive people (*Human Immunodeficiency Virus*) are pregnant women. Prevalence in this group is geographic location-related. In Africa it amounts to 30%, in Europe 0.4% and still, has an increasing tendency [15,3]. In Poland, till 2013, 17 565 persons were diagnosed with HIV infection, 8200 of which were women, 150 children. Most of children infections were due to the lack of mothers' diagnose [16].

The most frequent route of HIV transmission is via hetero and homosexual contacts, however, routes via blood and blood products, placenta and breast-feeding by HIV-positive mothers are also crucial. About 90% of children HIV infections are mother-to-child transmissions [15,3]. The risk of mother-to-child transmission is 15-30%, factors that increase the risk are: high level of viremia in mother's serum, preterm birth, vacuum-assisted vaginal delivery, amniotic fluid release 4h before the delivery. Most of vertically transmitted infections (70%)

occurs during perinatal period [15]. According to the Polish AIDS Society recommendations, HIV tests should be performed up to 10th week of pregnancy, and between 33th and 37th week of pregnancy. It is also recommended that pregnant woman's partner be tested for HIV [16].

Among others, following symptoms of primary HIV are present in mother: rapid weight loss, dry cough, recurring fever, night sweating, malaise, enlargement of axillary, arm and neck lymph nodes, diarrhoea, white spots on the tongue and in pharynx, pneumonia, headaches, muscle and joint pain. The disease may become a chronic, barely symptomatic infection and then, from a not treated, symptom-free interval carrier-state change into AIDS (*Acquired Immunodeficiency Syndrome*) [3].

HIV infection in infants does not cause congenital disorders and clinical symptoms usually occur during first months after the birth and can be in two forms. The first is the infection with rapid progression to AIDS when clinical symptoms such as: fatty liver and spleen, haematological disorders, recurrent bacterial infections, pneumonia develop in the first year of the child's life. The second form is represented by slowly progressing infections manifested by lymphocytic interstitial pneumonia and cardiomyopathy [7].

According to the Minister of Health ordinance of October 4th 2012 [17] on standards for medical procedure about healthcare services in the field of perinatal care taken over the woman during pregnancy, natural birth, postpartum period and infant care, the diagnostics of HIV in pregnant women during the first trimester of pregnancy is performed in Poland. The Polish Gynaecological Society recommends to perform these tests in 33-37th week of pregnancy in women with a higher risk due to the population or individual factors of HIV acquisition [8].

Hepatitis B (HBV), Hepatitis C (HCV) infections

Hepatotropic viruses, which include the *Hepatitis C virus* (HCV) and *Hepatitis B virus* (HBV) are the causes of diseases known as hepatitis C or hepatitis B. According to NIH data, the number of cases of hepatitis C and hepatitis increases every year [5].

Viral hepatitis may change into a chronic form or lead to a permanent carrier-state which is often a cause of the liver cirrhosis and death, mainly due to primary liver cancer [18]. It is estimated that in Poland 1.4% of people are infected with Hepatitis C virus. The risk of infection in women of childbearing age and the risk of transmission of the virus through vertical route are increasing whilst the frequency of mother-to-child transmission is estimated to be 6.2% [19]. The factors that increase the risk of transmission are: high level of viremia, concomitant HIV infection, infection of PBMCs, female gender of a child and the presence of identical alleles of HLA-DR in the mother and child [20].

HIV and HCV co-infection during pregnancy may bear serious consequences: HIV co-infection associated with high levels of HCV-RNA promote the transmission of HCV. The risk of preterm birth in HIV-positive mothers rises. Women with HCV/HIV co-infection should be categorised as a group of high risk of complications [21].

The course of HCV infection in pregnant women is mild, however decrease in ALT activity in the third trimester of pregnancy and increased aminotransferase levels after birth are observed. There are 3 models of the disease course in children with HCV infection via vertical route. The first one which concerns 20% of causes is related with spontaneous elimination of HCV and the recovery. The second one which concerns 50% of children with HCV infection via vertical route is characterised by prolonged, asymptomatic course with a periodic HCV replication. The third one is a prolonged, active hepatitis with persistent HCV replication, increased ALT activity and liver enlargement [20].

Roberts et. al. in their study concerning mother-to-child hepatitis C infection state that mother-to-child transmission of HCV is a rare case [22]. Apart from the care of hepatologists given for the mother, a fast diagnosis of HCV in child is possible if mother was diagnosed with the infection. As HCV antibodies of the mother penetrate the placenta, diagnosis of HCV vertical infection in the first year of the child's life requires HCV viral level testing. The basis for diagnosis of infection in children is a double detection of HCV replication by PCR or persistent presence of HCV antibodies in blood serum for more than 18 months. Exclusion of HCV infection in the child whose mother is infected with the virus requires at least two negative results of HCV RNA or elimination of HCV antibodies prior the 18th month [5,7].

HBV infection concerns about 5-10% of worldwide population [23,7,24]. The prevalence in Europe ranges from 2% to 7%, in pregnant women is 0.6-1% [23].

Perinatal HBV infections can occur in children of mothers who suffer from acute hepatitis B during pregnancy and infants born to mothers infected with a chronic HBV. The highest risk of vertical transmission occurs in the case of acute hepatitis especially during perinatal period. The high risk of transmission also concerns pregnant women that suffer from chronic HBV, in which a high level of HBV viremia, high concentration of Hbs antibody and presence of Hbe antibody are diagnosed. The highest risk of transmission - 70-90% occurs during

natural childbirth. The infant HBV infection most frequently occurs in pregnant women with HBeAg antibodies and HBV viremia higher than 10^8 copies/ ml. In the acute phase of infection the pregnant woman suffers from alleged flu-like symptoms, such as: fatigue, malaise, nausea, vomiting, loss of appetite, then jaundice, stool discoloration and darkening of the urine. A chronic infection in pregnant woman and HBV infection in infants is often asymptomatic [18]. Immediately after, infants born to mothers infected with HBV should be provided with both active and passive methods of prevention (specific serum HBV - HBIg and vaccine against HBV). Later, child vaccination series are continued. These procedures protect the child in more than 95% against HBV infection [23]. Studies have shown that the HBV virus is present in human milk, but there is no consensus that it may transmit the infection to the child. The risk of infection is present when the child has damaged mucosa in mouth, or when woman's nipples become ruptured during breast-feeding so the fluid with a high concentration of HBV virus is released [18].

HBV infected woman should contact infectious disease specialist about her decision of becoming pregnant. HBsAg test should be performed in every pregnant woman and in case of negative result it should be repeated before the childbirth. [25].

Varicella zoster virus - the etiological factor of varicella

Varicella, a disease caused by *Varicella zoster* (VZV) which belongs to *Herpesviridae* family, is one of the most frequent childhood illnesses. *Varicella zoster* virus is a highly infectious disease - infectivity up to 90%. Primary varicella zoster virus infection occurs between 4 and 9 years of age mainly by droplet contact, directly by the exposition to infected objects. A mother-to-child vertical transmission is also possible [26]. The prevalence in pregnant women is very low because most of adult people recover from the disease in childhood [27]. It is estimated that 5% of women at the age of 15-40 have no VZV antibodies [28].

Zoster virus (VZV) infection during pregnancy may lead to severe consequences: congenital varicella syndrome before 18th week of pregnancy and zoster virus infection in infants. 350 to 500 of such cases are registered in France every year [29].

Primary varicella zoster virus infection in pregnant women may be transferred to child at every moment of pregnancy however, negative effects in foetus are related to the time of infection. In the first 20 weeks of pregnancy the transmission concerns 1-2% of pregnancies but the consequences are severe. Viral replication during organogenesis causes foetal death, spontaneous miscarriages or severe congenital disorders known as congenital varicella syndrome. Children are diagnosed with: scars, losses of skin tissue, malformation of hands, arms and legs, lack of or malformation of digits, malformation of eyeballs, cataract, chorioretinitis, retinitis, ptosis and strabismus. Abnormalities in the nervous system (cerebral cortex atrophy, microcephaly, seizures, abnormal autonomic nervous system activity) are also observed. Deaths among children with congenital varicella syndrome occur most often because of secondary infections or organ failure. About two cases of death due to congenital varicella syndrome are noted in Poland every year [30].

The occurrence of varicella symptoms in pregnant woman from 5 days before to 2 days after the childbirth is related with 17-30% risk of infant infection and occurrence of varicella of severe course (extensive rash, pneumonia, hepatitis) due to the lack of mother's antibodies [28,30].

In case of exposure of pregnant woman to varicella virus her VZV immunity profile should be specified. The proven presence of VZV IgG antibodies indicates prior contact with the virus and thus, immunity to infection. The lack of antibodies presence indicates the lack of immunity and possibility of varicella development [28]. The analysis shows that about 95% of women who declare they have not suffered from varicella in childhood or they are not sure about this fact, have antibodies. In Poland, children above 9 months of age who have not suffered from varicella and women, who plan pregnancy and have not suffered from varicella are advised to be vaccinated against varicella [28,31]. Passive immunity acquisition- human immunoglobulin with a high titre of antibodies against varicella (VZIG varicella zoster immunoglobulin) is administered up to 96h after direct contact: to the infant of mother, who has fallen ill with varicella 5 days before to 2 days after the birth; premature babies born after 28 weeks of pregnancy whose mothers have not suffered from the disease and had not been vaccinated; premature babies born before 28th week of pregnancy or with a birth weight <1000 g, regardless of the history of the mother. VZIG administration is recommended in pregnant women who have not suffered from the varicella and had not been vaccinated against VZV due to risk of occurrence of pneumonia, which is 10%. Immunoglobulin administration not always provide a protection against the disease but may alleviate the course of varicella [31].

Measles virus - the etiological factor of measles

Due to the long period of introduction of vaccination against measles, this disease, which is caused by the *Measles virus* (MV) is rare in adults but if occurs it is related to frequent complications. These are: pneumonia, acute otitis media, keratitis with impaired vision, encephalitis, subacute sclerosing encephalitis, inflammation of the liver and biliary tract, pericarditis and miscarriage. Bacterial infection may also occur (*Streptococcus pneumoniae*, *H. influenzae*, *Staphylococcus aureus*). Pregnant women and immunosuppressed patients are significantly exposed to complications and severe course of the disease [32,33].

Complications are significantly more severe in pregnant women. Infection with the virus during pregnancy may have harmful effect on life and health both on mother and foetus. In a study conducted by Centrum Zwalczania i Zapobiegania aChorobom (the Center for Disease Control and Prevention) on a group of 58 pregnant women who suffered from measles, 15 of them suffered from pneumonia, and two died because of the infection. The most frequent observed negative consequence of infection was preterm birth (13 out of 58 women) [34]. As Seneczko states, during the epidemic of measles in Japan (2000-2001) out of 8 pregnant women, in 3 of 4 cases of infection before 24th week of pregnancy miscarriage or stillbirth occurred. In infants the infection is connected with high risk of neurological complications [32]. The infection with measles during pregnancy increases the risk of preterm birth, miscarriage and may also be a reason of the low birth weight [35].

The laboratory criterion that confirms the diagnosis of measles is detection of MV IgM antibodies in non-vaccinated patients in latest period i.e. at least 8 weeks before the onset of symptoms, the confirmation of at least 4-fold increase in IgG antibody titer or the detection of the virus in clinical material [36].

Myxovirusparotitis - etiological factor of epidemic parotitis

Epidemic parotitis (mumps) is an acute infectious disease caused by *Myxovirusparotitis*, whose the only natural vector is human. The infection is spread by droplet contact or by a contact with dry drop of infectious material. Infection spreads on parotid glands, but during viremia it may attack meninges or exocrine glands (pancreas, testes, ovaries) [37] neurological complications occur in 1-70% of unvaccinated persons. During the acute course of epidemic parotitis inflammation of the ovaries may occur in 5-7% of adult women, and in 31% of women over 14 years of age mammitis is diagnosed. Pregnancy does not seem to affect the course of epidemic parotitis however, if the infection occurs in the first trimester there is a risk of miscarriage [34]. Spontaneous miscarriages occurred in 1/4 of pregnant women who suffered from the epidemic parotitis during the first 12 months of pregnancy [37]. Epidemic parotitis in pregnant women during the first trimester may be related to damage to the central nervous system of the foetus.

In 2012, in Poland, 2779 cases of epidemic parotitis were registered (prevalence: 7.2 per 100 000) and the number was higher by 7.5% contrary to the previous year. In 2012, 1 177 women suffered from the disease (prevalence: 5.9 per 100 000) [38]. In 2013, 2436 cases were registered (prevalence: 6.3 per 100 000), wherein 194 women between 20 and 44 years of age became infected which stands for 8% of all cases of epidemic parotitis [39]. According to preliminary data from the NIH in 2014, the number of cases of epidemic parotitis in Poland amounted to 2508 (prevalence: 6.5 per 100 000.) [5].

The only effective method of reducing the number of cases of epidemic parotitis is use of active immunoprophylaxis that to a large extent limits the risk of the disease-related complications. Vaccination performed three months before planned pregnancy provide a protection against the disease. Vaccination of pregnant women is not recommended [34,37].

Influenza virus

Influenza if cause by influenza viruses A and B that form one type and influenza virus C which differs typically, all of them however are included in *Orthomyxoviridcie* family. It has been indicated that type A with subtypes H1N1, H2N2, H3N2 and H1 N2 are transferred between humans [40]. The infection occurs via droplet contact and via direct contact with infected person or surface.

Pregnant women form a particular group of risk - the disease is diagnosed as frequently as in the general population but complications occurs more often. The factors that increase the risk of severe course influenza with complications in pregnant women is related to physiological changes. These are: changes in the immune system (weakening of cell-mediated immunity, selective suppression of Th1 lymphocytes and progressive depletion of B cells in pregnancy with maintaining their functionality expressed by the normal antibody production), increased cardiac ejection fraction, increased oxygen consumption, decreased volume of lungs. Cell-mediated

immunity which is related to the activity of cytotoxic T lymphocytes plays a crucial role in protection against the infection [41]. Infection with influenzaviruses during pregnancy increases the risk of miscarriage, preterm birth, cardiac arrhythmia, disorders of the nervous system and digestive system of the foetus, and low birth weight baby [41,42].

Material that is suitable for the diagnostic is: a swab of throat and nasopharynx, throat washings, aspirate from the nasopharynx, bronchial lavage, cerebrospinal fluid, pleural middle ear biopsy, serum. The material used in direct identification of viral antigen and the nucleic acid should be sampled up to three days from the onset of the first symptoms [42].

Prophylaxis of influenza is mainly based on vaccination. Inactivated viral vaccines are safe and do not cause complications either in the mother or foetus [43]. Optimal time for vaccination against flu is before conception but there are no contraindications to vaccination of women during the second and third trimester of pregnancy [42]. Vaccination against flu in pregnant women as well as in women during postpartum period and in those who plan to become pregnant ensure the implementation of the so-called "cocoon strategy". ("strategia kokonu"). This strategy is based on vaccination in immediate environment of the patient that is susceptible to infection but cannot be vaccinated because of the young age or chronic medical contraindications for vaccination. Currently registered and available vaccines against influenza in Poland are possible for use in patients at 6 months of age, whereas influenza occur in younger infants, moreover, they are much more prone to complications, hospitalization and death. Mother's antibodies play a protective role arising from vaccination or natural course of infection and they are transferred to child by transplacental route (IgG) and during breast-feeding (IgA). The duration of protection obtained passively from the mother appears to be directly dependent on the concentration of antibody in cord blood and it is considered to last no longer than six months. Children who have had higher levels of antibodies in the cord blood suffered from the disease later in life and the course of the disease was mild contrary to children with lower levels of antibodies obtained from mothers [41]. Since 2005, WHO has recommended vaccination for all pregnant women in a particular influenza season. Vaccination against influenza in pregnant women is also recommended the American College of Obstetricians and Gynecologists [41].

Knowledge about influenza and its consequences during pregnancy, and vaccines against the disease is low among pregnant women. According to the Italian National Vaccination Plan for 2012-2014 vaccination during pregnancy is recommended. Unfortunately, less than 6% of the surveyed women realized how important vaccinations against the flu are. Research shows that in order to increase the approval of influenza vaccines, it is necessary to extend the knowledge among pregnant women in the field of influenza and its complications [44].

Apart from vaccination, additional activities in the prevention of influenza taken by women during pregnancy include: avoiding contact with infected persons or with increased risk of infection, avoid staying in crowded places, leading a healthy lifestyle, choosing suitable clothes and a diet rich in vegetables and fruits [42].

Summary

Among infections caused by "other" pathogens of TORCH panel, virus infections dominate in pregnant women. These infections may significantly influence women's health and pose a risk to the foetus. Primary infections of pregnant woman cause most severe complications for the foetus. Intrauterine infections caused by pathogens "others" are one of the main causes of preterm births, miscarriage and congenital malformations of the central nervous system, heart defects, haematological disorders and psychomotor retardation in the infants. Screening tests for known pathogens in pregnant women, vaccinations and avoiding certain risk factors for perinatal infections by women are key factors in prevention of infection.

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