Translated from Portuguese to English - www.onlinedoctranslator.com

RCMOS – Multidisciplinary Scientific Journal O Saber.

ISSN: 2675-9128. Sao Paulo-SP.

Year IV, v.1, n.1, Jan./Jul. 2024. | submission: 06/10/2024 | accepted: 06/12/2024 | publication: 06/14/2024

AN APPROACH TO CONGENITAL DISEASES AND THEIR DUE REPERCUSSIONS

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Summary

Congenital infections are the main determinants of permanent disability in children and have a major impact on morbidity and mortality and treatment costs. Among the main infections that can cause complications in pregnancy, the following stand out: toxoplasmosis, rubella, cytomegalovirus, syphilis, zika virus, herpes, hepatitis. These infections can cause morphological changes in fetal tissues or organs, therefore, early identification and treatment can reduce maternal-fetal transmission and/or reduce the impact on the fetus. Therefore, the objective of this study was to carry out an updated review on congenital infections, highlighting epidemiological, diagnostic and treatment aspects. This is a literature review, and the following databases were used to construct the text: SciELO, PubMed, VHL and Google Scholar. Therefore, prevention, early diagnosis of congenital infections and other actions aimed at adequate treatment of women and their children, with the integration of health programs and local surveillance systems, are extremely important for public health.

Keywords: Congenital anomaly, perinatal congenital infections, infected birth canal.

Abstract

Congenital infections are the main causes of permanent disability in children and have a major impact on morbidity and mortality and treatment costs. Among the main infections that can cause complications in pregnancy are: toxoplasmosis, rubella, cytomegalovirus, syphilis, zika virus, herpes, hepatitis, acquired immunodeficiency syndrome and parvovirus B19. These infections can cause morphological changes in fetal tissues or organs, thus, early identification and treatment can reduce maternal-fetal transmission and/or decrease the impact on the fetus. Thus, the aim of this study was to conduct an updated review of congenital infections, highlighting epidemiological, diagnostic and treatment aspects. This is a literature review, and for the construction of the text, the following databases were used: SciELO, pubmed, BVS and Google academic. Therefore, prevention, early diagnosis of congenital infections and other actions aimed at the adequate treatment of women and their children, with the integration of health programs and

local surveillance systems are extremely important for public health.

Keywords:Congenital anomaly, perinatal congenital infections, infected birth canal.

Introduction

Congenital infection is a disease transmitted from mother to baby during pregnancy, intrauterinely or transplacentally, and can have consequences for the child after birth. Congenital or perinatal infections, which occur during the baby's transition through the infected birth canal or through breastfeeding, can occur in up to 10% of births

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The main congenital infections are: toxoplasmosis, rubella, cytomegalovirus, viral hepatitis, HIV and syphilis. In addition to these, other rarer maternal infections can also lead to congenital infection, such as parvovirus B19 infection, herpes simplex, varicella-zoster, Zika virus, dengue fever and Chagas disease.

The acronym TORCH was initially proposed to group some congenital infections: toxoplasmosis, others (parvovirus, malaria, Chagas disease), rubella, cytomegalovirus and herpes. This acronym later became known as TORCHS, adding hepatitis B and C, HIV and syphilis.

During prenatal care, serological screening for these diseases during pregnancy is essential for early diagnosis and treatment, when available. There is no international consensus on which of these diseases should be screened for during prenatal care. The Ministry of Health in Brazil recommends that serological screening be carried out for all pregnant women, at the beginning of pregnancy and in the third trimester, for the following diseases: syphilis, HIV, toxoplasmosis and hepatitis B. Other congenital infections should be screened for as suspected by the condition maternal or fetal clinic.

Mostly, congenital infections are transmitted vertically transplacentally, however in some diseases, transmission occurs during childbirth, as is the case with HIV infection, hepatitis B and C, herpes simplex, Coxsackie and malaria. Transmission through breastfeeding is rare and has only been seen in HIV and hepatitis B infection and in cases of breast lesions caused by syphilis or herpes simplex. Although there are studies of vertical transmission during breastfeeding, breastfeeding is only prohibited in cases of maternal HIV.

The following article aimed to describe congenital diseases, analyzing information and disseminating pathological characteristics about the repercussions of congenital infections.

Methodology

This is a qualitative narrative review study, suitable for discussing the repercussions of congenital infections. It consists of a comprehensive analysis of the literature, which the method was based on by retrieving articles indexed in the databases of PubMed, Lilacs, SciELO, Latindex and other literature pertinent to the topic, during the month of June 2024, with the period reference over the last 15 years.

The indexing terms or descriptors were used: congenital infection, congenital transmission, serological screening, isolated or combined. The criterion chosen for inclusion of publications was to have the expressions used in the searches in the title or keywords, or to have it explicit in the abstract that the text relates to aspects linked to congenital infections. The excluded articles did not meet the established inclusion criteria and/or were duplicated, that is, publications restored in more than one of the databases. Dissertations and theses were also excluded. After the target information was retrieved, the titles and abstracts were initially read. Subsequently, the complete reading of the 30 texts was carried out. As axes of analysis, we initially sought to classify the studies according to sampling particularities, delimiting those whose samples are from pathological aspects and those whose samples are from congenital repercussions. From there, the analysis of the theoretical foundation of the studies continued, as well as the observation of the general characteristics of the articles, such as year of publication and language, followed by their objectives. Finally, the methodology used, results obtained and discussion were assessed.

Results and discussion

The search for articles that made up this study identified 155 references regarding the repercussions of congenital infections in the aforementioned databases, of which 30 publications were included in the review. Among the selected studies, 28 articles have a theoretical approach, 1 has a cross-sectional design, two articles deal with a case study. The prevalence of publications in English was observed, representing 84% of the total, when compared to Spanish (9.6%) and Portuguese (6.4%).

Toxoplasmosis

Toxoplasmosis is the disease caused by Toxoplasma gondii, an obligate intracellular protozoan. This protozoan has a life cycle with two hosts: felids as definitive hosts (hosts the adult parasite, in its reproductive form) and humans, birds or mammals, as intermediate hosts (hosts the parasite in its young or asexually reproducing form). Furthermore, they present an evolutionary cycle with three main forms:

• Tachyzoites: present in the acute phase or re-examination of the disease, they present high multiplication rates and are capable of infecting the central nervous system, eyes, muscles and placenta.

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- Bradyzoites: they are found in the tissues of humans and all intermediate hosts, presenting have low replication activity. In immunocompromised hosts, they can transform back into tachyzoites.
- Sporozoites: they are found inside oocytes, formed exclusively in the feline intestine and are eliminated through feces, infecting the intermediate host. It is the most resistant form of the parasite and can remain in the environment for years. Transmission of Toxoplasma gondii to humans can occur through the ingestion of oocytes (sporozoites), present in food, water, contaminated soil, or through the ingestion of tissue cysts (bradyzoites), present in raw or undercooked meat. We call this transmission "oral". Therefore, transmission can occur through tachyzoites during acute infection, through blood transfusion, contact with secretions and excretions or transplacentally.

Vertical transmission occurs mainly transplacentally during acute maternal infection, through the passage of tachyzoites through the placenta. Furthermore, vertical transmission can also occur during childbirth and breastfeeding if the woman is in the acute phase of the disease. Although transplacental transmission is rare in cases of reactivation of maternal infection, it can occur if the pregnant woman has severe immunosuppression.

It is important to highlight that transplacental transmission is greater the higher the gestational age. In the first quarter, the transmission rate is 14%, reaching 60% in the third quarter. On the other hand, the severity of the disease is greater when vertical transmission occurs early in pregnancy. As the transmission rate decreases by around 50% in pregnant women treated during pregnancy, prevention, tracking and diagnosis of this disease is essential in order to avoid the complications of congenital toxoplasmosis.

Primary prevention of toxoplasmosis is done by avoiding the ingestion of bradyzoites present in meat from contaminated animals (intermediate hosts) and oocytes (sporozoites) present in fruits, vegetables, soil or water contaminated with feces from contaminated cats (definitive hosts).

The main primary prevention measures for toxoplasmosis are:

- Correct hand hygiene before meals, after handling garbage, having contact with animals and handling raw food and meat.
- Handle earth or soil with gloves and, afterwards, clean your hands.
- Consume only filtered or boiled water.
- Properly clean fruits and vegetables (soak in chlorinated solution for 10 minutes).
- Freeze meat before consumption.
- Do not consume raw, undercooked or undercooked meat.
- Do not consume raw milk and dairy products.
- Avoid contact with stray animals.
- Feed cats with food and do not allow them to eat raw meat or game.
- Avoid handling domestic cat litter boxes and contact with cat feces.

Diagnosis of toxoplasmosis during pregnancy

Acute infection during pregnancy is generally asymptomatic, toxoplasmosis screening must be done by requesting serology (IgG and IgM) for all pregnant women, as per guidance from the Ministry of Health. The periodicity of screening varies depending on the epidemiological profile of each region, but serology for toxoplasmosis should be done at least in the first, second and third trimesters for susceptible pregnant women. In regions where there are high rates of toxoplasmosis, serology should be performed every two months in susceptible pregnant women.

TOXOPLASMOSIS SEROLOGY IN PREGNANCY

IG G	IgM	Diagnosis	Conduct
-	+	Susceptible	Prevention



+	-	Immune	Pre Christmas habitual
-	+	False position tivo	Repeat so- rology in 2 months
+	+	Infection acute re- cent	Admin- tion of spirituality ramycin

TREATMENT OF TOXOPLASMOSIS IN PREGNANCY

Toxoplasmosis treatment should be instituted if acute infection is suspected or confirmed during pregnancy. Early treatment within three weeks of maternal infection reduces the risk of fetal infection.

Therefore, the main approach in a case of recent infection is prophylaxis for congenital toxoplasmosis, with maternal administration of spiramycin at a dose of 3g/day, orally, and screening for fetal infection. This is applied in cases of maternal seroconversion (IgM and IgG) initially negative that become positive throughout pregnancy, or suspected recent infection (IgM and IgG) positive up to 16 weeks with low avidity. In cases where there is doubt whether the infection is recent or old, such as when the first serology with positive IgG and IgM is performed after 16 weeks and the avidity test is no longer reliable, the pregnant woman should then be managed as recent infection, treat with spiramycin and investigate fetal infection.

Spiramycin does not cross the placental barrier, but it acts to reduce the risk of transplacental passage of the parasite, preventing fetal infection. Therefore, the diagnosis of congenital toxoplasmosis (fetal infection) must be made by searching for Toxoplasma Gondii DNA by PCR in a sample of amniotic fluid, collected by amniocentesis from 16 to 18 weeks for all cases of maternal seroconversion or suspected seroconversion. recent infection. If the fetal infection test is negative, continue spiramycin until delivery. If fetal infection is confirmed, start treatment with **sulfadiazine**, **pyrimethamine**It is**folinic acid**(triple scheme) from 16 to 18 weeks until the end of pregnancy. It is important to be careful not to start the triple regimen in the first trimester, due to the risk of teratogenicity of these medications.

CONGENITAL TOXOPLASMOSIS

An infection during pregnancy can result in miscarriages or fetal deaths. If the pregnancy progresses, it is important to note that the majority of children are asymptomatic at birth.

Symptomatic ones are generally infected during the first trimester of pregnancy and may present systemic manifestations, such as hepatosplenomegaly, jaundice and hemolytic anemia; neurological; Hearing Loss; and ophthalmological deficits.

In congenital toxoplasmosis, a rare occurrence occurs, but toxoplasmosis can be differentiated from other congenital infections through Sabin's tetrad:

Tetrad of Sabin
Chorioretinitis
Calcifications cediffuse rebrais
Hydro/microcebankrupt
mental retardation

CYTOMEGALOVIRUS

Human cytomegalovirus (CMV) is a DNA virus from the Herpesviridae family and its only host is humans. This virus has a high latency capacity, that is, it is not eliminated by the body and therefore can reactivate in cases of modification of the immune response, such as during pregnancy, in the use of immunosuppressive medication and in patients with HIV. Furthermore, reinfection with new viral strains may occur.

Cytomegalovirus (CMV) infection presents a high risk of transmission to the fetus, as it leads to harmful effects on the fetus, mainly on the central nervous system and is the most common cause of congenital viral infection in the

Cytomegalovirus (CMV) infection in immunocompetent patients is mostly asymptomatic or presents as a mononucleosis-like condition, with fever, asthenia, myalgia and cervical lymphadenopathy. Maternal transmission occurs through interpersonal contact with infected body fluids, such as saliva, blood, urine and genital secretions. Vertical transmission occurs mainly transplacentally, but can be transmitted during birth if there is contact with contaminated secretions and during breastfeeding, as CMV is excreted through breast milk.

Currently, maternal primary infection during pregnancy increases the risk of vertical transmission, which can reach up to 40% and lead to serious fetal compromise. Furthermore, once again, the higher the gestational age, the greater the risk of vertical transmission and the risk of fetal involvement is inversely proportional to the gestational age. Furthermore, recurrent maternal infection has less devastating effects on fetuses and, in these cases, the majority are asymptomatic at the time of birth.

The diagnosis of maternal CMV infection is carried out by serology with the search for specific IgG and IgM antibodies. However, serological screening during pregnancy is controversial and is not recommended by the Ministry of Health as routine screening, as immunity does not protect the fetus from reinfection or reactivation and there is no effective treatment during pregnancy. Therefore, serological tests for CMV are recommended during pregnancy if there are any ultrasound changes suggestive of congenital infection.

If the pregnant woman has negative IgG and IgM serology, she is susceptible to primary infection and must take greater care with hygiene measures. Now, pregnant women with positive IgG and negative IgM serology do not have permanent immunity, as reinfection or reactivation may occur during pregnancy.

When the serology is IgG and IgM positive, and there is no previous negative serology to prove seroconversion, an IgG avidity test must be requested to assess whether the infection is recent (less than four months if the avidity is low). < 30% less old (more than six months if avidity is high, > 60%).

Currently, there is no effective treatment for fetal CMV infection during pregnancy, as the use of antiretroviral drugs has not been shown to be effective in reducing vertical transmission or the severity of the disease in newborns.

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Congenital cytomegalovirus infection is usually asymptomatic, in 90% of cases. Symptomatic patients were generally infected in the first trimester of pregnancy. The clinical picture is based on systemic, neurological, ophthalmological and auditory manifestations.

The most prevalent signs at birth are cholestatic jaundice, petechiae and hepatosplenomegaly. Sensorineural deafness can manifest itself at birth or later, this is the main sequelae of the disease. In fact, cytomegalovirus is the most common infectious cause of deafness in childhood. A finding that distinguishes CMV infection from other congenital diseases is the presence of periventricular intracranial calcifications, which may be associated with hearing loss and petechiae.

In this congenital infection, serology is not a good method, but viral research in body fluids is. Infected patients secrete the viruses into body fluids for years after infection. The presence of cytomegalovirus in the newborn's urine or saliva within the first three weeks of life closes the diagnosis of congenital infection.

The complementary assessment, based on the search for signs, must be carried out with a blood count, liver function tests, neurological imaging tests, CSF collection, fundus examination and hearing screening.

The treatment is controversial in the literature. The Ministry of Health recommends treatment with ganciclovir for 6 weeks in newborns with confirmed infection, symptomatic and with evidence of CNS involvement, hearing changes and/or chorioretinitis.

RUBELLA

Rubella is an acute, highly contagious exanthematous disease that mainly affects children and adolescents. The importance of rubella is mainly due to the occurrence of congenital rubella syndrome (CRS), which affects the fetus and newborn of mothers infected during pregnancy, which is a nationally notifiable disease.

Due to vaccination campaigns for the entire population, this disease has been eradicated in Brazil since 2008, according to the World Health Organization (WHO), and is no longer part of mandatory screening during prenatal care.

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The etiological agent of rubella is an RNA virus from the togavirus family and humans are the only known host. Maternal transmission occurs through intimate and prolonged interpersonal contact, through droplets of secretion from the nasopharynx. Vertical transmission occurs transplacentally during the first maternal infection, with extremely serious fetal involvement occurring when the infection occurs in the first trimester. After 20 weeks of gestation, there are no reports of manifestations compatible with CRS.

Rubella is asymptomatic in more than 50% of infected adults. When symptomatic, the main symptoms are: maculopapular erythema with centrifugal distribution, low fever, headache, anorexia, mild conjunctivitis, runny nose, cough and lymphadenomegaly

Rubella is prevented by vaccination in children and adults, providing lifelong immunity. In turn, the vaccine should not be given to pregnant women, children under 12 months and immunosuppressed people, as it treats - if live attenuated virus. Therefore, you must wait a month to get pregnant after receiving the rubella vaccine. Pregnant women inadvertently vaccinated in the first trimester should be informed that the possibility of teratogenicity is only theoretical and there is no indication for termination of pregnancy.

The vaccine is available to children at 12 months, within the triple viral and at 15 months in the tetra viral. Unvaccinated teenagers and adults up to 29 years of age should receive two doses and, for individuals aged 30 to 59, only one dose is required. The diagnosis of rubella during pregnancy is made by serology with the search for specific IgG and IgM antibodies. Serology should be requested in case of suspected rubella during pregnancy or contact with a suspected person.

If pregnant women have negative IgG and IgM serology, they are susceptible and should receive vaccination during the postpartum period. When a susceptible pregnant woman comes into contact with an individual with rubella, she must receive hyperimmune immunoglobulin within six days of contact. It is worth mentioning that the use of hyperimmune immunoglobulin can attenuate the clinical manifestations of rubella, but it does not prevent viremia or vertical transmission.

Pregnant women with positive IgG and negative IgM serology have permanent immunity and must follow the pre-routine Christmas. When serology is IgG and IgM positive for rubella in the first trimester, but there is doubt as to whether the infection is recent (not symptomatic), an IgG avidity test should be requested to clarify the diagnosis. If the avidity is low, the infection is recent (less than three months if the avidity < 60%), if it is high, it is old (more than three months if the avidity > viral

Congenital rubella

The classic hallmark of congenital rubella is heart disease. Congenital rubella syndrome is associated with heart disease, cataracts and bilateral sensorineural hearing loss.

Regarding the diagnosis, the presence of IgM antibodies confirms the infection, but, once again, the absence does not rule it out. We can also isolate the virus in nasopharyngeal secretion, cerebrospinal fluid and urine. In addition, complementary exams and clinical history finalize the diagnosis. The importance of the echocardiogram is highlighted.

Unfortunately, in this case, there is no specific treatment for congenital infection, it must be aimed at the complications of the disease.

ZIKA VIRUS

The Zika virus is an arbovirus (transmitted by mosquito bites) of the Flavivirus genus and presents benign behavior, low virulence and low lethality. It is known that the main route of transmission of the Zika virus is through the bite of the aedes aegypti mosquito, the same vector of dengue, chikungunya and yellow fever. Furthermore, sexual transmission has been verified and the virus has already been identified in blood, semen, urine, saliva and breast milk. Since 2015, vertical transmission of the Zika Virus has been demonstrated. Since then, suspected or confirmed Zika virus infection during pregnancy and congenital Zika virus syndrome (CZS) are compulsory notification.

in Brazil. There are still no reports of transmission during childbirth and breastfeeding.

The Zika virus causes asymptomatic infection in 80% of cases. When symptomatic, it presents with exanthematous disease in 90% to 100% of these cases. Low fever, myalgia, mild to moderate arthralgia, conjunctivitis, headache, pruritus, ganglion hypertrophy and neurological impairment may also occur.

Congenital Zika virus infection syndrome (SCZ) can manifest with microcephaly, microphthalmia, congenital clubfoot, arthrogryposis, hydrops, fetal growth restriction, miscarriage and fetal death. The main ultrasound signs during pregnancy are: microcephaly, periventricular calcifications, ventriculomegaly, microphthalmia, congenital clubfoot and fetal growth restriction.



Characteristics Zika virus

Microcephaly

Clubfoot con-Genit

Microcephaly is defined by a head circumference more than two standard deviations below the mean for gestational age or sex.

However, since 2016, after the Zika virus outbreak, Brazil has defined microcephaly as boys measuring 31.9 cm or less and girls measuring 31.5 cm.

It is evident that the Zika virus has a high affinity for nervous tissue and microcephaly occurs mainly when the infection appears in the first trimester. Furthermore, the fetal prognosis can be made according to the degree of microcephaly, as the more severe the microcephaly, the greater the neuropsychomotor impairment.

During pregnancy, there is no recommendation for a universal screening test for Zika virus infection. However, in the presence of an exanthematous disease during pregnancy, a rapid test for dengue, Chikungunya and PCR for Zika virus must be requested up to the 5th to 7th symptoms. Furthermore, differential diagnosis must be made with other exanthematous diseases (TORCHS, varicella-zoster, parvovirus B19). It is known that serology for Zika virus has low specificity, since IgM antibodies show cross-reactivity with other diseases, such as dengue. Once the diagnosis of infection by the Zika virus has been established, fetal morphology and vitality should be studied, in addition to serial monthly ultrasound examinations, in order to identify fetal involvement by the Zika virus.

On the other hand, the pregnant woman may not present symptoms and the suspicion of congenital infection with the Zika virus occurs due to the diagnosis of microcephaly on routine ultrasound. In these cases, it is recommended to perform IgG and IgM serology for Zika virus, dengue and Chikungunya and rule out other causes of microcephaly (serology for syphilis, toxoplasmosis, rubella, CMV and varicella-zoster), in addition to an evaluation with a geneticist.

When diagnosed with congenital Zika virus syndrome, the pregnant woman must be referred to a tertiary center. Because treatment for congenital syndrome caused by the Zika virus is not available, childbirth and the postpartum period maintain a normal routine and breastfeeding is not contraindicated in these cases.

Upon suspicion of the disease, the child will undergo an audiological evaluation, neuroimaging and serology of other congenital infections for differential diagnosis. Confirmation can be done by RNA detection (RT-PCR) and/or IgM serology by ELISA. Once again, there is no specific treatment and she must have multidisciplinary monitoring for early stimulation and to reduce the loss of neuropsychomotor development.

PARVOVIRUS B19

Parvovirus B19 is a single-stranded DNA virus that has tropism for rapidly dividing cells, such as those in the bone marrow. This virus is transmitted by respiratory, blood and transplacental routes. Transplacental passage occurs in around 25% of cases of infection during pregnancy and is more serious when it occurs in the first half of pregnancy.

In children, Parvovirus B19 causes erythema infectiosum, a self-limited disease characterized by malar erythema fever (slapped face) and rash on the trunks and extremities. In adults, the infection is usually asymptomatic. Erythrocyte aplasia and chronic infection in the bone marrow of immunocompromised individuals may also occur.

Acute infection during pregnancy can lead to transplacental transmission to the fetus, but, in most cases, there are no fetal manifestations. However, in some cases, cytotoxicity occurs in fetal erythropoiesis, resulting in fetal anemia, non-immune hydrops fetalis, early pregnancy loss and fetal death. Despite this, this situation can resolve spontaneously in utero, when the manifestations are not severe.

The diagnosis of maternal infection during pregnancy is made by serology for Parvovirus B19, evaluating IgG and IgM antibodies, in the case of a suspected case of parvovirus during pregnancy, recent exposure to the virus or symptoms compatible with acute infection.

When the pregnant woman is IgM and IgG negative, she is susceptible and should be advised not to have contact with people with symptoms suggestive of parvovirus. If IgM is negative and IgG is positive, the pregnant woman is immune and there is no risk of fetal infection.

Intrauterine infection is very rare and there is no prenatal serological screening. Most cases are transmitted during birth through contact between the newborn and lesions in the maternal genital tract.

The pathology is exclusively symptomatic and can manifest as localized, neurological or disseminated disease. The main characteristics of this are skin lesions and conjunctival hyperemia

The gold standard diagnostic method is viral isolation and culture in tissues and blood. Additional tests must be requested for clinical evaluation. Treatment is with acyclovir. It is noteworthy that more important than treatment is prevention, which must be carried out in all infected pregnant women, through treatment of maternal lesions, prevention of recurrence, indication of cesarean section in case of active genital lesions at the time of birth. childbirth and suspending breastfeeding if the breasts are compromised.

In pregnant women, treatment is done with acyclovir, trying to avoid treatment in the first trimester, although studies do not show an increased risk of fetal malformations. The dose for the treatment of acute injuries in pregnant women is 400mg, 3x a day, or 200mg, 5x a day, orally, for seven to ten days.

Prevention of congenital herpes must be carried out in all pregnant women who have already been infected. To achieve this, acyclovir should be used around the 36th week of pregnancy, even in the absence of symptoms, in pregnant women with previous genital herpes, to prevent recurrence at term and avoid cesarean section. If the pregnant woman presents the first episode of genital herpes at the time of birth or up to six weeks before, it is recommended to perform a cesarean section, although there is no randomized study that shows the effectiveness of a cesarean section in preventing transmission of neonatal herpes. In the face of recurrent genital herpetic infection at the time of birth, cesarean section is also indicated. Furthermore, people with active injuries should not touch the baby. The infected newborn must be kept in contact isolation.

Conclusion

Regarding the information discussed in this study, it can be seen that the prevalence of congenital infections is high, with prenatal care in Brazil being essential regarding prevention, early diagnosis of congenital infections and other actions aimed at adequate therapy for women and their children, with the integration of health programs, local surveillance systems working to interrupt the transmission chain, allowing the institution of early treatment and a better quality of life for children.

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