Infectious diseases in the neonatal period: A literature review

https://doi.org/10.56238/sevened2023.007-089

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ABSTRACT

Neonatal infectious diseases are pathologies that affect newborns, usually in the first four weeks of life. They are transmitted through breastfeeding or during pregnancy. They are congenital when transmission occurs transplacentally. An example of this is cytomegalovirus, toxoplasmosis, syphilis, and rubella, acquired during childbirth (less than 48 hours of life), caused by group B Streptococcus and Escherichia coli or nosocomial (more than 48 hours of life) caused by acquisition during the period of stay in the Neonatal Intensive Care Unit due to healthcare-associated infections (HAI). In this context, the study aims to highlight the main infections that occur in the neonatal period, understand the pathogenic process, clinical manifestations, diagnosis, and treatment of infectious diseases. The methodology used was an exploratory literature review, with a qualitative approach, through bibliographic research of books and articles, using the Lilacs, PubMed and SciELO databases. Examples of this class of pathologies include early or late neonatal sepsis and viral infections such as neonatal herpes, hepatitis B, HIV, Zika, Chikungunya and dengue. Thus, it is concluded that a rapid diagnosis and treatment is important, as these infections evolve to severe conditions due to the immaturity of the neonate's immune system. Prevention includes proper prenatal care, maternal immunization, and hygiene precautions during childbirth and after birth.

Keywords: Newborn, Neonatal infections, Pregnancy, Neonatology.

1 INTRODUCTION

Neonatal infections are acquired during a patient's hospital stay. Law No. 9,341, of January 6, 1997, describes nosocomial or nosocomial infection as any infection acquired in a hospital environment or after medical discharge (BRASIL, 2007).

According to the National Health Surveillance Agency (ANVISA, 2013), the term nosocomial infection has been replaced by Health Care-Related Infection (HAI), which more adequately defines the way in which the infection is acquired. This change in nomenclature allowed the addition of new studies on neonatal infections, expanding their scope and evaluating not only infections originating in the hospital environment, but all those related to health care. After the new nomenclature, it became evident that, even with the new proposal to expand the studies, HAI are translated as infections that occur exclusively within the hospital environment (FERNANDES, 2011).

Examples of this class of pathologies are neonatal sepsis, which appears early or late, viral infections such as neonatal herpes, hepatitis B and C, HIV, Zika and Chikungunya, in addition to dengue. It is important to establish the diagnosis in order to immediately start treatment, as these infections are usually severe due to the immaturity of the neonate's immune system. Prevention includes adequate prenatal care, maternal immunization, and hygiene precautions during childbirth and after birth, according to the Pan American Health Organization (PAHO, 2016).

It is known that colonization of the fetus occurs in the uterus, transplacental route, or by ascension via the maternal genital tract. In intrauterine acquired infections, the most common route is transplacental hematogenous after maternal infection occurs. Intrauterine infection of the fetus occurs due to the rise of bacteria through the genital tract from contamination and colonization, resulting in fetal aspiration of contaminated amniotic fluid, which leads to pneumonia and sepsis. To be considered an early infection, clinical or laboratory diagnostic evidence is required within a period of less than 48 hours and that the pregnant woman has associated risk factors, which are: ruptured pouch after a period of more than or equal to 48 hours, cerclage, labor at less than 37 weeks of gestational age, fetal procedures in the last 72 hours, urinary tract infection without prior treatment or with treatment less than 72 hours before, maternal fever less than 48 hours before delivery, colonization of the pregnant woman by Streptococcus spp (group B) and chorioamnionitis. Based on this, neonatal HAI are classified as a relevant problem, as control depends on simple measures to be performed, which apply to the pregnant woman, the hospital environment, the multidisciplinary team, and the newborn himself. Thus, health actions are proposed to reduce the morbidity and mortality of these patients (MAGALHÃES, 2016).

According to the Ministry of Health, in newborns up to 28 days old, infections are considered hospital-based, with the exception of infections that are transmitted transplacental and those related to the rupture of ovular membranes. In addition, it is necessary to take into account the common

mechanisms of infection, such as the administration of contaminated fluids, such as blood products, medications, parenteral nutrition, breast milk and milk formulas (FERNANDES, 2000).

In this sense, the objective of this study is to highlight the main infections that occur in the neonatal period, to understand the pathogenic process, clinical manifestations, diagnosis and treatment of infectious diseases.

2 MATERIAL AND METHOD

The study was developed through an exploratory literature review, with a qualitative approach, through bibliographic research of books and articles, using the Lilacs, PubMed and SciELO databases, available in Portuguese and English, without date limitation. The descriptors used were: neonatal infection, neonatology, nosocomial infection, newborn, infections during pregnancy.

3 DEVELOPMENT

3.1 HISTORY OF NEONATOLOGY

At the beginning of the nineteenth century, newborn care was performed by mothers and midwives, which justifies the fact that mortality rates were high in that period. In addition, the low birth weight in neonates was justified by the natural fragility of some babies. Death was also expected for premature newborns and those with malformations. There was a concept that these children were the result of natural selection, which was responsible for selecting children who were less adapted to survival. Care for these individuals began to emerge in 1892, due to high mortality rates and low birth rates. The French obstetrician, Pierre Budin, created the first childcare outpatient clinic at the Charité Hospital in Paris, being responsible for the emergence of the principles and methods that formed the basis of Neonatology (AVERY, 2007).

After this initiative, the care of neonates was continued through the creation of incubators, which arose due to the encouragement of obstetrician Stéphane Etienne Tarnie, in Paris, an innovation that reduced the mortality rate among premature and low birth weight newborns by 50%. For four decades, at Martinité Hospital, newborns, who were previously destined for death, had a greater chance of survival. The importance of caring for newborns led to an improvement in diet and oxygen administration techniques in 1934, with the Hess Oxygen Box, which explicitly reduced the mortality of these individuals (BRAGA; SENA, 2013).

Thus, Dr. Pierre Budin was considered the first creator of modern Neonatology, based on the principle of temperature control and maintenance, prevention of infections associated with health care, breastfeeding and the constancy of mothers' care for premature infants (PACHECO, 2000).

3.2 INFECTION AND/OR CONTAMINATION OF THE NEWBORN

Infections in newborns are very common, especially when they are hospitalized in Neonatal Intensive Care (NICU) environments and, according to the Pan American Health Organization (PAHO, 2016), the most common forms of contamination occur when newborns are still in utero, through maternal infections that occur through the transplacental route, when premature rupture of membranes occurs for a period longer than 18 hours without delivery occurring. During childbirth, the infection can occur through direct contact with maternal secretions and, after birth, they can also be contaminated by contact with the mother, family members, a multidisciplinary team of health professionals, or even by the disproportion between the number of hospitalized newborns and the number of health professionals assigned to the care of these children. number of hospitalized patients greater than the capacity of the hospital environment and through objects used for physical examination, such as thermometers, stethoscopes, incubators.

Factors that favor greater maternal colonization, such as recurrent urinary tract infection without adequate treatment and cerclage, are considered to be at risk for the development of infection in the maternal-fetal binomial (BRASIL, 2014).

Cerclage is defined as the surgical procedure used to attempt to correct cervical isthmus incompetence, in order to prolong pregnancy and, thus, reduce the occurrence of spontaneous abortions and premature births (MACHADO et al., 2017). The term cervical isthmus incompetence refers to the inability of the cervix to prolong pregnancy in the absence of signs and symptoms related to imminent labor in the second trimester of pregnancy (NELSON et al., 2009).

The risk factors for neonatal infections inherent to the newborn are: low birth weight, lower immune defense, need for invasive procedures, and alteration of the microbiota by microbiological agents acquired in the hospital environment (PAHO, 2016).

Other forms of transmission/infection of the newborn, such as contaminated blood products and fluids, medications, parenteral nutrition, milk formulas, and breast milk, should also be considered. Respiratory route, in rooming-in, outbreaks of viral infections by adenovirus, influenza, respiratory syncytial virus can be mentioned. Warning that, of all the colonization mechanisms, contact continues to be the main and most common mechanism of contamination/infection of the newborn and that the manifestation of signs and symptoms related to the infection varies according to the degree of immunity of the individual, virulence of the infecting microorganism and the qualitative and quantitative characteristics of the pathogen's inoculum (BRASIL, 2014).

3.3 NEONATAL, EARLY AND LATE SEPSIS

It is a clinical syndrome characterized by systemic signs of infection, accompanied by bacteremia in the first month of life, followed or not by positive blood culture, related to reduced

immune functions and the immaturity of the innate immunity of the neonate. Neonatal sepsis is classified as early, in terms of the moment of onset, when the clinical picture appears in the first 72 hours of life; being late, when it begins after 72 hours of life (PROCIANOY, 2019).

> Neonatal sepsis is a clinical syndrome with hemodynamic changes and other systemic clinical manifestations resulting from the presence of a pathogenic germ (bacteria, virus or fungus) in normally sterile fluid, such as blood or cerebrospinal fluid, in the first month of life. Neonatal sepsis is an important cause of neurocognitive sequelae and neonatal mortality (SHANE, 2017).

According to MOREIRA (2012), early diagnosis and immediate specific treatment of neonatal sepsis significantly reduce morbidity and mortality rates, which will vary according to the pathogen involved, immunological status, and the presence of complications associated with the condition. Clinical manifestations may be minimal or nonspecific. However, in newborns who do not have symptoms but have risk factors for the development of infection in clinical practice, empirical antimicrobial treatment is instituted.

The main risk factors for the development of neonatal sepsis, early or late, are considered the following: chorioamnionitis, rupture of the amniotic membrane (MPR) for more than 18 hours, colonization by Streptococcus agalactiae, *preterm delivery*, *bacteriuria, colonization by* group B Streptococcus (GBS) low maternal age (< 20 years), previous NB with GBS infection. As the clinical manifestations are nonspecific, the diagnosis is thorough, since there are clinical signs such as apnea, respiratory distress, cyanosis, tachycardia or bradycardia, poor perfusion or shock, irritability, lethargy, hypotonia, convulsions, abdominal distension, vomiting, food intolerance, gastric residue, hepatomegaly, unexplained jaundice, thermal instability, petechiae or purpura. Thus, the following clinical signs for sepsis should be considered: thermal instability, respiratory distress, hypotonia and seizures, irritability and lethargy, gastrointestinal symptoms, and jaundice (PINHEIRO et al., 2016).

Early neonatal sepsis is related to factors of the peripartum, prenatal or delivery period, resulting in multisystemic involvement, resulting from germs present in the maternal genitourinary tract in the vast majority, such as *group B Streptococcus* (full-term newborn) and *Escherichia coli* (premature newborn (PROCIANOY, 2019).

According to Silveira (2012), the diagnosis of early neonatal sepsis should be anticipated due to its high morbidity and mortality, based on maternal and neonatal risk factors, clinical manifestations of the newborn, and laboratory tests, such as: blood culture (gold standard), blood count, C-reactive protein (CRP), cerebrospinal fluid, urine, among others. And in order to confirm the diagnosis of neonatal sepsis, the presence of three or more clinical signs of the newborn or at least two of these clinical signs, associated with maternal risk factors, are necessary. Therefore, the diagnosis is clinical and laboratory.

Late-onset neonatal sepsis occurs due to postnatal factors, newborns who require prolonged hospitalization and lack procedures used in intensive care units (ICU), such as catheter insertion, endotracheal intubation, venipunctures, parenteral nutrition, horizontal transmission and, among hospital microorganisms, the main agents involved are: Gram-negative bacteria, *Staphylococcus aureus*, *Coagulase-negative Staphylococcus* and fungi. Newborns who remain in prolonged hospitalization are often affected. (VILAÇA et al., 2023).

Treatment is empirically established with the use of antibiotics such as ampicillin and gentamicin, which will be instituted within twenty-four hours after the onset of symptoms of the clinical picture of infection, regardless of the results of laboratory tests. The antibiotic regimen is commonly used because it covers the germs that cause neonatal sepsis. When the result of the blood culture is obtained, through the antibiogram test, the selection of the most appropriate antibiotic for the treatment and its time will be directed, based on the type of pathogen, location, evolution, and repetition (VILAÇA et al., 2023).

More important than treating neonatal sepsis is preventing its onset, which requires a multifactorial approach to causes. Firstly, investment should be made in the eradication of the main risk factor related to it: prematurity (GUINN; GIBBS, 2002).

3.4 CONGENITAL INFECTIONS OF THE S.T.O.R.C.H + Z GROUP

The acronym S.T.O.R.C.H was created with the aim of bringing together the main infectious diseases capable of causing disease in pregnant women and fetal malformations. The infections that are part of the S.T.O.R.C.H group are: Syphilis, Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex, being expanded to S.T.O.R.C.H + Z due to the epidemic of Zyca Virus in Brazil.

3.4.1 Toxoplasmosis, Congenital

Toxoplasmosis is a common parasitic infection in humans, caused by a protozoan called Toxoplasma gondii and is a public health problem. These infections are more prevalent in tropical regions (AFONSO et al., 2013), and their incidence is related to the proportion of women who become pregnant, the competence of the immune system, and the rate of exposure to the agent during pregnancy (PEYRON et al., 2017). In Brazil, the risk of uninfected women acquiring toxoplasmosis during pregnancy and transmitting it to the fetus is high, and the severity of this infection will depend on the gestational period in which the woman is when infected.

When the infection occurs in the first trimester of pregnancy, miscarriage of the fetus may occur. When the infection affects pregnant women in the second or third trimester, it is possible to have prematurity, retinochoroiditis, cerebral calcifications, microcephaly, eye changes, mental disability and hydrocephalus. (FELDMAN; KELLER; BORGIDA, 2016; LEVINE et al., 2017; OZ,

2017). The diagnosis is monitored by the obstetrician in the prenatal period with the performance of serology for toxoplasmosis through the request of IgG, IgM, IgA, which are extremely important in the prevention of acute toxoplasmosis (NEU; DUCHON; ZACHARIAH, 2015).

3.4.2 Rubella

Rubella virus infection during pregnancy, especially in the first trimester, leads to miscarriages, stillbirth, and a newborn with a series of malformations known as congenital rubella syndrome (CRS) (PAHO, 2010). Infection in the first trimester of pregnancy causes a fetal infection rate of 80% to 100%. When pregnancy progresses to the 16th week, fetal infection rates drop by 10% to 20%, rising again to over 60% after the 30th week of pregnancy (CURTI et al., 2014). Diagnosis during pregnancy occurs through a screening that involves serology testing for rubella, requesting IgM and IgG (NEU; DUCHON; ZACHARIAH, 2015).

3.4.3 Citomegalovirus

Cytomegalovirus is a herpes virus that remains in its latent form, but during pregnancy it reactivates, causing a reinfection. It is transmitted at any stage of pregnancy or through the passage of the fetus through the vaginal canal, as long as the pregnant woman has viremia. Congenital herpes simplex infection leads to high morbidity and mortality of the newborn (DOLLARD; BIALEK; GROSSE, 2014). In the presence of an infected newborn, the clinical manifestations are: sensorineural hearing loss and neurological impairments in children (LEUNG et al., 2020). Maternal diagnosis can be made through cytomegalovirus (IgM and IgG) serology (ENDERS; CALVO, 2017).

3.4.4 Syphilis

Maternal and congenital syphilis is a major public health problem. In 2010, Brazil, in partnership with the Member States of the Pan American Health Organization, approved the Strategy and Action Plan for the elimination of mother-to-child transmission of Congenital Syphilis and HIV with the aim of reducing infection rates (COOPER et al., 2016). During pregnancy, syphilis is very harmful, as it is responsible for miscarriage, prematurity, fetal and neonatal death, and a large number of hospital admissions (BRASIL, 2019).

For the diagnosis, the pregnant woman undergoes serology during the first month, in the second month and during hospitalization for delivery. Obstetric ultrasonography aids in the diagnosis, detecting possible signs of fetal involvement such as encephalitis, bone deformities, intracranial, hepatic, cardiac, placental calcifications, and hydrops fetalis (MORSHED; SINGH, 2015; NEU; DUCHON; ZACHARIAH, 2015).

3.4.5 Zyca virus

The Zyca virus is a flavivirus, of the Flaviviridae family, emerging and responsible for a worldwide epidemic (BRASIL, 2016). It is known for its repercussions during the gestational period, with microcephaly being the most common manifestation, especially when the infection occurs in the first trimester (BRASIL, 2020). Diagnosis is made by performing IgG and IgM serology and polymerase chain reaction (PCR) (MUNOZ-JORDAN, 2017

3.5 VIRAL INFECTIONS/ARBOVIRUSES

During pregnancy, infection with the Chikungunya virus can occur, but cases of miscarriage are rare. If maternal infection occurs in the intrapartum period, there may be transmission to the newborn by transplacental route, and there is no evidence that delivery by cesarean section modifies transmission (BRASIL, 2014). The newborn remains asymptomatic in the first days of life, but from the 4th day onwards, he begins to present fever, irritability, pain syndrome, edema in the extremities, skin lesions and desquamation, hematological disorders, diarrhea, hemorrhagic syndromes, meningoencephalitis, encephalitis, refusal to feed. In general, infections that occur in the perinatal period sometimes leave neurological sequelae that reach neuropsychomotor retardation, and can progress to death (BRASIL, 2022; SREEKANTH et al., 2021; KUMAR et al., 2019; TORRES et al., 2016).

The infection caused by the dengue virus occurs vertically, presents a risk of miscarriage if it occurs in the first trimester and, if it occurs in the third trimester, increases the chance of premature birth (BRASIL, 2016).

In HIV infection, factors such as advanced disease of the pregnant woman, CD4 count below 200 cells/mm3 and high plasma viral load, vaginal delivery, chorioamnionitis, premature delivery and breastfeeding are necessary for transmission (PAHO, 2010).

The transmission of Hepatitis B within the uterus depends on the amount of virus circulating in the pregnant woman's blood and corresponds to the main risk factor for chronic infections in adults (BROWN et al., 2016). The hepatitis B virus can cause chronic infections and lead to cirrhosis and hepatocellular carcinoma (LIU; KAO 2017). Maternal-infant transmission of the hepatitis B virus is the main cause of acute or fulminant hepatitis B in early childhood (SOUTO, 2016).

4 FINAL THOUGHTS

Prenatal care is extremely important for maternal-fetal health. It is important to emphasize the importance of prevention, adequate treatment for pathologies of the gestational period, identification of early diagnosis of congenital infections and adequate guidance for these pregnant women through

health programs and surveillance systems, with the aim of interrupting the chain of transmission, allowing a better quality of life for pregnant women and their children.

Among the healthcare-associated infections (HAIs) in the neonatal period, it was possible to observe that sepsis is the most important of them and the most commonly found microorganisms are Staphylococcus aureus, coagulase Staphylococcus and E. coli. Infections/colonization mainly affect premature infants, due to the immaturity of the immune system. These infections in the neonatal period constitute a relevant problem in public health, a fact that requires feasible measures that are often simple to be applied in the hospital environment and that are capable of reducing the morbidity and mortality of newborns.

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