ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 07, Issue, 12, pp.18098-18101, December, 2017

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

MICROCEPHALY TRACKING ON ULTRASONOGRAPHIC EXAMINATIONS IN NEWBORNS

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ARTICLE INFO

Article History:

Received 15th September, 2017
Received in revised form
19th October, 2017
Accepted 25th November, 2017
Published online 30th December, 2017

Key Words:

Probiotics,
Lactobacillus,
Antibacterial activity,
Bacteriocin.

ABSTRACT

The purpose of this manuscript was to discuss the importance of ultrasound examinations in the screening of microcephaly in newborn babies. It was carried out a research using bibliographic and documentary analysis. Results of this study indicate the relevance of the creation of instruments that can help health professionals in the correct diagnosis of conditions related to the presence or influence of microcephaly in Brazil and other countries. As conclusion, in addition to the available techniques, it is necessary to use appropriate diagnostic tools to obtain good results from the screening actions and clinical evaluations.

Citation: Jaciara Lucena de Moraes, Elenir Rose Jardim Cury Pontes, and Valdir Aragão do Nascimento, 2017. "Microcephaly tracking on ultrasonographic examinations in newborns", *International Journal of Development Research*, 7, (12), 18098-18101.

INTRODUCTION

Microcephaly is a congenital anomaly where a baby's head is smaller compared with other babies of the same sex, gestational age and ethnicity, that is, the cephalic perimeter does not develop in the size considered normal. Nowadays epidemic outbreak caused by Zika virus is highly contagious and has spread to other parts of the Brazil and others coutries. Microcephaly associated with Zíka virus contagion whose main transmission vector has been the Aedesaegypti mosquito. Due to the great expansion of the zika virus and the increase of cases of microcephaly, the Ministry of Health of Brazil declared the event a public health emergency of national concern (KINDHAUSER MK) Microcephaly when observed at birth is called congenital. On the other hand, when observed during the first year of life, it is called postnatal microcephaly. Microcephaly when it presents genetic factors is called genetic microcephaly, however, when it has other triggering factors it is called environmental or external microcephaly. The diagnose microcephaly in the infant can be made during pregnancy, through an ultrasound examination or after the childbirth, through the measure of the head circumference and examinations, such as tomography and magnetic resonance (National). Diagnostic ultrasonography is an ultrasound-based diagnostic imaging technique used to visualize subcutaneous body structures. The diagnosis of microcephaly disease is performed through ultrasonography, mainly in the second gestational trimester, during which it is possible to measure the cephalic perimeter of the fetus. Although ultrasonograph is an imaging test considered to be simple and inexpensive to operate, it requires great skill and knowledge on the part of the operator. Faced with this new scenario to consider a baby with microcephaly, on January 3, 2016, the Brazilian Government changed the evaluation criteria of the cephalic perimeter from 33 cm to 32 cm, so fewer cases would no longer be suspect.

In view of the above, it is necessary to carry out a study that analyzes the impact of the evaluation criterion of the cephalic perimeter.Faced with this situation, the objective of this study was to carry out a detailed investigation and monitoring of microcephaly cases in live births in Brazil.

Microcephaly Prognosis, Causes, Symptoms, And Diagnosis

Microcephaly is a rare neurological condition in which an infant's head is characterized by reducing the cephalic perimeter with neurological disorders that decreases the

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cerebral cortex. It is a clinical observation, rather than a specific diagnosis. Microcephaly may also be related to proteins involved in DNA repair and mitotic components (YANG *et al*., 2012). According to Leal (2005), microcephaly is a clinical sign found in several disorders with environmental or genetic etiology. On the other hand, although there is a search to understand the genetic causes and bases of microcephaly, there are still many unexplained cases, which suggests that microcephaly needs to be further studied (Nakayama *et al.* 2015). In fact, there is progressive microcephaly that is a heterogeneous condition, and its causes include mutations of genes associated with the proper functioning of neurons and primary autosomal recessive microcephaly that are related to a moderate intellectual disability (Zhang et al., 2014). According to Arboleda et al. (2015) mutations of histone acetylation genes cause various abnormalities, including microcephaly.

There is primary microcephaly and genetic known as Vera or True, which is related to disorders without any other neurological changes, malformations, or genetic syndromes such as Down Syndrome and Criduchat Syndrome. It is characterized by two principal features, microcephaly present at birth and retarded brain growth, that is, brain growth is slow and should be from 1,200 to 1,500 grams, however no more than 500 to 800 grams (LOPES, 2015). Microcephaly of non-genetic or secondary causes are called microcephaly Cranioestenosis. Its is caused by harmful agents that reach the intrauterine fetus, especially in the first trimester of pregnancy. The use of chemical agents are coming from the mother, or from diseases such as smallpox, rubella, exposure to ionizing radiation.Such factors cause premature fusion of the cranial sutures before brain development preventing brain expansion and proving the skull cap deformity (LOPES, 2015).

As the skull is smaller than normal (smaller than 33 cm of head circumference), microcephaly compromises the development of the child's brain. The abnormality is related to different degrees of mental retardation, motor, balance and speech problems, as well as the development of seizures. According to studies, 90% of individuals with microcephaly have some degree of mental retardation. (NUNES et. al., 2016)

Microcephaly and Zika virus in Brazil

Confirmation of the first cases of Zika fever in Brazil was made in May 2015, initially in the Northeast when several patients had symptoms of fever, joint pain and other symptoms in the northeastern region. As the tests for the detection of Dengue and Chikungunya were both negative, the serology of some patients using reverse transcription polymerase chain reaction was performed, in which it was possible to detect the Zika virus (ZANLUCA e*t al.,* 2015). In Ceara, state of Brazil, the relationship between the Zika virus and the onset of microcephaly disease was only confirmed when tissue and blood samples from a baby were compared (MINISTÉRIO DA SAÚDE, 2015). The highest risk is related to the first trimester of gestation. In fact, it is a new scientific and worldwide situation, encouraging several studies in the search for understanding the transmission of the virus and its functioning in the human organism in order to understand its relation with microcephaly disease. In view of the above, there is a worldwide concern in the fight against the main transmitting agent, the mosquito Aedesaegypti.

In Brazil, according to the Ministry of Health (2016), microcephaly can be diagnosed 24 hours following birth, performing routine physical examinations in search of possible congenital malformations. Microcephaly can be detected and diagnosed also in the prenatal period when the pregnant woman undergoes medical follow-up and performs Ultrasonography examinations. After the child is born, a measurement of the cephalic perimeter is made, and newborns with a cranial perimeter equal to or less than 32 centimeters can be diagnosed with microcephaly. The unborn child with suspected congenital malformation is submitted to imaging and neurological examination. Transfontenela Ultrasonography is the first choice exam and the most suitable for the diagnosis of the disease (MINISTÉRIO DA SAÚDE, 2016).

The main reasons for the cause of microcephaly are: a) Syndromes or genetic problems such as Down syndrome. In relation to the genetic syndrome, there may be malformations in other parts of the body due; b) Infections suffered by the mother during pregnancy, such as arubola, cytomegalovirus, toxoplasmosis, syphilis zika; c) Exposure of the mother to teratogenic agents during pregnancy (radiation, chemical substances, alcohol consumption or drugs); d) Craniosynostosis or cranioestenosis: premature closure of baby's fontulas, where the initial problem is with the bones of the skull and not with the brain; e) Malnutrition, phenylketonuria or poorly controlled diabetes in the mother during gestation; f) Injury or trauma to the baby's brain, whether or not it is due at birth, in which case microcephaly only arises as the baby grows (BABY CENTER BRAZIL, 2016).

Although there is no specific treatment for microcephaly disease, in Brazil (Ministry of Health (2016)) the initial fight is the national mobilization to eliminate mosquito-borne outbreaks. These actions are being carried out and monitored by the Unified Health System (SistemaUnico de SaúdeBrasileiro - SUS), which developed a Protocol on Health Care and Response to the Occurrence of Microcephaly Related to Zika Virus Infection to early identify the disease and to assist in the care of these babies and in the follow-up of the mothers. Change in the diagnosis criterion of microcephaly made by the Brazilian Federal Government was initially adopted in the state of Pernambuco, but extended to the states of the Brazil. In thesis, with the reduction of the cranial perimeter from 33 cm to 32 cm, tfewer cases would no longer be considered suspect. According to pediatric infectologist Maria Angela Rocha, coordinator of the Oswaldo Cruz University Hospital (HUOC) in Recife, calcifications in the brain that usually happens after infectious processes were only observed in a few patients with cerebral perimeter between 32 cm and 33 cm (COSTA, 2015).

Zika virus is a flavivirus transmitted by mosquitoes. On April 18, 1947, fever developed in a rhesus monkey that had been placed in a cage on a tree platform in the Zika Forest of Uganda. The monkey had symptoms such as fever, headache, joint pain, among others. (DIAGNE e*t al.,* 2015). According to research carried out by Faye et al. (2013) mosquitoes by which the Zika virus is transmitted are the Aedes species, Ae. Furcifer, Ae. Taylori and Ae. Luteocephalus and Cercopithecusaethiops, Erythrocebus monkey paws, and also by domestic mosquitoes such as Aedes and Aegypti, Ae. Hensilli. The first isolated case in humans was described in

eastern Nigeria in 1954, later in Africa, Asia, Cote d'Ivoire, Egypt and other parts of Central and West Africa. From the first report of infection by Zika virus, few cases until 2007 had been reported in Asia and Africa, was when a major outbreak began on the island of Yap in Micronesia in the year 2013 and in French Polynesia at the beginning of 2014 (BUATHONG et al., 2015). The Zika virus family Flaviviridae and genus Flavivirus in its cycle covers Aedes mosquitoes and their transmission in epidemic has been increasingly present. Besides the Zíka virus, there are also epidemics of Dengue and Chikungunya caused by the same vector (BARONTI *et al.,* 2014).

Humans when infected with Zika virus present a moderate elevation of the temperature from 37.8º C to 38.5º C, presenting joint pain, muscle pain, headache, pain in the eyes and rashes. The diagnosis of people infected with Zika virus is difficult, since the symptoms are similar to those of influenza, usually only the presence of the virus is detected in the acute phase of the disease. Although there are no reports of cases related to hemorrhagic signs, however, neurological changes and complications have been reported (GOURINAT e*t al.,* 2015). According to research by Gourinat et al. (2015) biological detection is basically done by reading the ribonucleic acid (RNA) of the virus in a serum using reverse transcription Polymerasechainreaction (PCR). It should be noted that Immunoglobulin (IGM) against the virus can also be detected by the Enzyme-Linked Immunosorbent Assay (ELISA). It has been challenging to accurately detect the Zika virus because of the low virus presence in the blood, the cross-reactivity of the antibodies and their nonspecific aspects related to other viruses, including dengue.

Researchers from Brazil and Latin America, both with extensive experience in the epidemiology of congenital malformations, suggest that the evidence that Embryopathy due to ZIKV virus is responsible for cases of microcephaly is questionable. For this reason, the prestigious Latin American Collaborative Study of Congenital Malformations has published in its website a series of technical notes in which it shows the difficulty in definitively establishing the association among microcephaly and ZIKV virus. So, it proposes as an ideal method a case-cohort study with a flow chart that includes the investigation of STORCH infections and other possible teratogens such as Fetal Alcohol Syndrome and the dozens of genetic syndromes, from chromosomal diseases identified by the karyotype, such as the microdeletions and microduplications identified by the techniques from genomic to monogenic syndromes identified by the techniques called nextgenerationsequencing (BRUNONI et al., 2016).

Ultrassonography examination

Ultrasound examination is a method based on the effect of the interaction of mechanical waves with body tissues. Ultrasonic waves vibrate at 20,000 cycles or more per second and propel themselves through the tissues. Ultrasonography has signs of variable intensities and is associated with the effects of the interaction of a sound wave with the medium in which it propagates, that is, whether the medium has a good ability or not to reflect the propagated sound. Ultrasound examination is a method based on the effect of the interaction of mechanical waves with body tissues. Ultrasonic waves vibrate at 20,000 cycles or more per second and propel themselves through the tissues. Ultrasonography has signs of variable intensities and is associated with the effects of the interaction of a sound wave with the medium in which it propagates, that is, whether the medium has a good ability or not to reflect the propagated sound. Ultrasound examinations do not use ionizing radiation, thus there is no radiation exposure to the patient. Because ultrasound images are captured in real-time, they can show the structure and movement of the body's internal organs, as well as blood flowing through blood vessels. (CHAMMAS & CERRI, 2009). Ultrasonography is the method used to estimate fetus measurement during gestational period in several countries (TUNON et al., 2002). In fact, the estimation of gestational age is extremely important to accompany fetal growth. In the first trimester of pregnancy it is possible to evaluate the length of the head circumference / buttock. On the other hand, the biparietal diameter and length of the femur can be measured in the second trimester of gestation (YOSHIZATO; SATOH, 2009).

As microcephaly arises because the brain stops developing, it becomes difficult to diagnose it. This requires more time for any anomaly to be observed. Thus, if the problem that originated microcephaly occurred in the first trimester of gestation, it is probable that in the second trimester of the morphological ultrasound examination, for about 20 weeks, the head size is still within the normal range, and only on ultrasound microcephaly is perceived, or even after birth.Microcephaly may only become evident after the baby is born. The baby may have a normal head circumference at birth and the head stops growing at the expected rate in the following months. As a result of these facts, it is for this reason that cephalic perimeter measurement is part of routine pediatric procedures (BABY CENTER BRASIL, 2016).

Final considerations

Research involving Zika virus infection and its relation to the onset of microcephaly disease outbreak are necessary for a better understanding of the dynamics of its transmission. Brazil faces an epidemic of the disease and little is known so far.It is fundamental to develop tools that can help researchers in the search for correct diagnoses in order to understand the aspects related to the disease, so that the data obtained in the research may, in fact, help in understanding the factors associated with the appearance of cases of microcephaly , as well as providing subsidies for an adequate prenatal follow-up protocol, especially in relation to ultrasonography. Because it is a worldwide public health problem, it requires studies and research, as well as an immediate search for solutions to combat the disease-enhancing agent, which justifies the benefit to the individual involved in the health-disease process.

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