Symptoms of Zika virus (ZIKV) infection are usually mild and do not require aggressive management. For the same reason detection of ZIKV is not routinely performed. Unfortunately, consequences of inborn infections can be grave and lead to permanent disabilities. Association between ZIKV infection and microcephaly in infants was observed during the recent outbreaks. Range of clinical implications caused by microcephaly differs depending on the severity of condition. As targeted therapy is not available, management of future mothers is mostly focused on prevention of the infection. Most cases of ZIKV transmission are caused by vectors, therefore adequate use of protection against mosquitoes is essential. Planning pregnancy should be postponed in case of suspected infection – for 8 weeks and 6 months for women and men, respectively. Confirmation of infection is possible by detection of ZIKV, ZIKV RNA or any other antigen in bodily fluids or tissue and serological testing. Management of children with microcephaly requires advanced diagnosis considering their development and neurological condition together with early implementation of psychomotor therapy. The gravity of ZIKV infections in endemic populations manifests the need of public health programmes concerning family planning and monitoring ZIKV expansion to new territories.
BACKGROUND

Zika virus (ZIKV) is a mosquito-borne flavivirus, first identified in Uganda in 1947 in monkeys by researchers monitoring yellow fever [1]. Later virus was identified in humans in 1952 in Uganda and the United Republic of Tanzania [2]. Outbreaks of ZIKV disease have been recorded in Africa, the Americas, Asia and the Pacific [1]. From the 1960s to 1980s, human infections were found across Africa and Asia, typically accompanied by mild illness [1]. The first large outbreak of disease caused by Zika infection was reported from the Island of Yap (Federated States of Micronesia) in 2007 [2]. The next epidemic of ZIKV infection was reported in 2015 in South and Central America and the Caribbean [1].

TRANSMISSION

Apart from spreading by vectors, vertical transmission is also possible if woman’s infection occurs short before or during pregnancy [3]. Research is ongoing to determine the possibility and characteristics of transplacental ZIKV transmission [3]. Although the virus can be present in breast milk, no transmission of ZIKV through breastfeeding has been reported up to date [3]. ZIKV transmission may also, though rarely, occur through blood transfusion from a person in the period of viremia or sexually [3]. The maximum period of ZIKV presence in semen has not been ascertained, however it was confirmed to last over two weeks post infection [3]. It was also found that ZIKV may be present in urine and saliva, but so far no infection caused by contact with these bodily fluids has been described [4].

SYMPTOMS, DIAGNOSIS AND TREATMENT

The incubation period of ZIKV disease is not clear, but likely to be a few days [5]. People usually do not present enough symptoms to be admitted to the hospital and mortality associated with ZIKV infection is relatively low [6]. For this reason, many people might not realize they have been infected [6]. Symptoms of ZIKV infection are similar to other viruses spread through mosquito bites, like dengue and chikungunya [5]. The most common symptoms of Zika include: fever, rash, general pruritus, subcutaneous bleedings, joint pain and conjunctivitis [5]. Other symptoms are muscle pain, headache and loss of appetite [5]. These symptoms are usually mild and last for 2-7 days [7].

Due to real-time reverse transcription PCR (rRT-PCR) detection of ZIKV RNA is possible in various fluids: in serum (up to 6 days), urine (up to 27 days), cerebrospinal fluid (up to 7 days), saliva (up to 13 days), and vaginal swab (up to 13 days) [8]. Around the fifth day of the disease specific antibodies in blood are detected, but serological diagnosis can be difficult due to presence of cross-reactions with other flaviviruses [8]. Positive results in immunofluorescence screening tests must be confirmed by neutralization test (Plaque Reduction Neutralization Test - PRNT) [8]. To confirm the infection it is preferable to prove at least a 4-fold increase in ZIKV neutralizing antibodies titer, serum should be collected twice [8]. Treatment is mainly symptomatic. Usually, symptoms disappear spontaneously without complications. However, higher incidence of Guillain-Barre syndrome during ZIKV epidemics on the islands of French Polynesia was reported [6]. The direct relationship between the infection and the syndrome has not been definitively confirmed [6]. Treatment of ZIKV infection includes administration of antipyretics, but use of nonsteroidal anti-inflammatory drugs, especially acetylsalicylic acid, is not recommended until the exclusion of dengue [9].

MICROCEPHALY

Microcephaly is a neurological abnormality, usually congenital and presented at birth. It is defined as the head circumference at least 2 SD smaller than average for sex and age [10]. There are two main groups of microcephaly causes: genetic disorders (syndromes related to chromosomal or single gene defects) and acquired brain damages (intrauterine injuries, vertically transmitted infections, drugs and other) [11,12]. It was observed that newborns with microcephaly were also small for gestational age [13].

The prevalence of microcephaly ranges from 2.0 to 12.0 per 10000 live births (USA) and 2.9 per 10000 live births (Europe). There has been observed a significant change in the number of newborns born with microcephaly in Brazil as the prevalence increased from 0.6 per 10000 live births in 2010 to 4.2-8.2% in 2012-2015 in consequence of the outbreak of Zika virus infections [14].

INFECTION DURING PREGNANCY

ZIKV infection in pregnant women does not usually cause any grave disorder to mothers. The clinical manifestation consists of fever, maculopapular rash, arthralgia, fatigue, general malaise and other symptoms characteristic for viral infections [8,15]. Increased risk of microcephaly was associated with infections in the first trimester of pregnancy, similarly to other viral factors of congenital neurological disorders like Cytomegalovirus or Rubella virus [12]. Some data suggest that neurological abnormalities associated with ZIKV were also observed in infections with later onset during the second and even the third trimester of pregnancy [15].

PRENATAL DIAGNOSIS

In Brazilian case series, newborns of women infected with ZIKV between 5th and 16th week of pregnancy were affected by microcephaly [16]. Moreover, ZIKV genome was detectable in amniotic fluid samples [16,17]. Fetal microcephaly is usually diagnosed in ultrasound at 32.3 ± 5.1 week of pregnancy, however earlier observations are possible [16,18]. The ultrasound examination may show additional brain abnormalities. Except from the microcephaly, diffuse parenchymal calcifications, ventriculomegaly, reduced gyriication and cerebellar hypoplasia were observed [1,18].

Neurological abnormalities typical for intrauterine ZIKV infection could be a cause of miscarriages or medical terminations of pregnancy [19,20]. Autopsies of infected fetuses confirmed microcephaly with fetal tissues positive
for ZIKV RNA, and viral antigens in glial cells and neurons [20].

CLINICAL IMPLICATIONS OF MICROCEPHALY IN NEWBORNS

Microcephaly is associated with various clinical problems which depend on how severe the microcephaly is [21]. Newborns with microcephaly may have developmental delay, intellectual disability, blurred vision, hypacusis, movement disorders, impaired coordination and balance, and difficulty swallowing [21]. Developmental delay concerns both speech and milestones such as sitting, standing or walking [21]. It is important to remember that severe microcephaly can be a life-threatening condition. It is very difficult to assess how advanced developmental disorder is and what kind of symptoms the child will present in future [21]. Because of this fact children with microcephaly should be checked up by doctors regularly [21].

MANAGEMENT OF NEWBORNS WITH MICROCEPHALY

Measurement of head circumference (HC), preferably within the first 24 hours of life, is the most common way of microcephaly diagnosis [21]. Specific growth charts are used for microcephaly assessment. The value for microcephaly on a HC centile chart is less than 3rd percentile or 2 standard deviations below the average [21]. There is no standard treatment for microcephaly. Procedures depend on how severe the microcephaly is. Children with mild microcephaly do not require any special care because their only symptom is smaller head size and they usually do not present additional clinical problems [21]. Newborns with severe microcephaly need early intervention which includes speech, hearing and physical therapies [21].

TORCHZ ACRONYM

Various observations suggest association between microcephaly and laboratory-confirmed ZIKV [13]. Detection of ZIKV specific IgM antibodies is an adequate method of congenital ZIKV infection diagnosis [13]. In Brazil significant association between epidemic of microcephaly and ZIKV infection was observed [13]. Therefore, it is suggested to extend the TORCH acronym [Toxoplasmosis, other infections such as Varicella-zoster virus, Syphilis, Parovirus B1, Rubella, Cytomegalovirus and Herpes simplex virus] to TORCHZ acronym in order to pay attention to a serious problem of congenital ZIKV infection [13].

RECOMMENDATIONS: PREGNANCY DURING ZIKV OUTBREAK

Prevention of ZIKV infection during pregnancy includes avoiding travel to endemic areas and avoiding transmission via mosquito bites. Protection should focus on choosing proper clothing, covering arms and legs, use of registered insect repellents and staying in screened-in or air-conditioned rooms [22]. Laboratory evidence for ZIKV infection in pregnant women include detection of ZIKV, ZIKV RNA or antigen in any fluid or tissue, and positive serological test towards ZIKV with negative dengue results [23]. In a pregnant woman with confirmed ZIKV infection frequent ultrasounds are advised in order to monitor fetal anatomy and growth every 3–4 weeks. Patients should be managed by a perinatologist and infectious disease specialist [22].

RECOMMENDATIONS: FAMILY PLANNING DURING ZIKV OUTBREAK

Both men and women are advised to postpone procreation after likely ZIKV infection. For women it is recommended to wait at least 8 weeks after exposure or onset of symptoms. In case of men longer period – 6 months – is preferred. Couples planning pregnancy should avoid nonessential travel to areas with Zika, seek medical advice from healthcare provider, and prevent mosquito bites by means of repellents. Risk of sexual transmission can be decreased due to use of mechanical barriers [24].

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REFERENCES


