

EDITORIAL
HUMAN TRANSMITTED DENGUE
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“Dengue is a viral disease transmitted by the bite of the Aedes aegypti mosquito; When the mosquito feeds on the blood of a person sick with dengue and then bites other people, it transmits this disease. Contagion only occurs through the bite of infected mosquitoes, never from one person to another, nor through objects or breast milk.”

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This is how the Dengue page begins on the Argentine Health Portal (www.argentina.gov.ar).

However, these concepts are – at best – misguided and/or outdated, and imply a dangerous omission, especially in times of epidemic.

Taking into account that 75-80% of the initial cases of dengue are asymptomatic (that is, they have not been studied or classified as such at the beginning), the lightness with which other forms of transmission other than the traditional sick person – mosquito – healthy person.

The World Health Organization issued a report on March 17, where projections indicated that the number of infected people annually would be around approximately 400 million, and 90 million would be symptomatic.

This means that there is a fairly high percentage of patients who are infected with the virus who do not present symptoms.

This makes the epidemiological situation very complex, because generally asymptomatic patients can become the drivers of infections; Not the symptomatic ones since these are the ones who will be consulting.

Having made these clarifications, we proceed to list and develop the different forms of human transmission of Dengue, confirmed to date.

- Vertical Transmission
- Transmission through Breast Milk
- Transmission by Sexual Contact
- Transmission from Laboratory Accidents
- Transmission by Transfusions
- Transmission by Transplants

VERTICAL TRANSMISSION

Dengue can be transmitted to the newborn in two ways, vertically and by horizontal contagion.

In highly endemic countries, the incidence of dengue during pregnancy is estimated to be close to 1%.

Regarding the maternal-fetal binomial, vertical transmission has been reported from 1.6% to 10.5% depending on the series and gestational age (at the end of pregnancy there is a greater risk).

If the infection is contracted in the first trimester, there is a risk of teratogenesis, abortion and poor obstetric outcomes; and if it is contracted in the third trimester there is a risk of preterm birth and low birth weight, in addition to a high possibility of neonatal dengue.

With respect to maternal health, there is an increased frequency of hemorrhagic complications during abortion, childbirth or cesarean section.

The transmission of dengue from mother to child during pregnancy generates reproductive or perinatal risks, which may occur without signs at birth in 80-90%, while 10-20% of newborns may present associated signs such as maculopapular rash, Hepatomegaly, lymphadenopathy, petechiae, presence of purpura or vesicles.

It has been related to a higher incidence in premature births, in newborns small for gestational age, and intrapartum hypoxia; In them, the risk of neonatal dengue will be 7 days before delivery.

Goncalves de Castro indicates that in Brazil the rates of infection, dissemination and vertical transmission of DENV-2 were demonstrated.

Symptoms in the newborn are variable, described even from 9 hours after birth to 11 days of life, with an average of 4 days.

Therefore, if a mother is suspected of having dengue, the newborn must be followed during the first two weeks of life.

In a study carried out in Mexico, it was observed that newborns presented variable clinical symptoms (from asymptomatic to severe dengue fever with signs of shock and hemorrhage); Thrombocytopenia, temperature alterations and other more non-specific manifestations were evident in the majority.

Diagnosis in the newborn is made based on serological methods (ELISA-IgM), viral culture and molecular techniques in accordance with the diagnostic criteria.

Within the methodology applied for diagnosis, the NSI viral antigen for dengue can be assessed as an early diagnosis and then the determination of IgM antibodies for dengue can be performed by MicroElisa.

The symptomatic treatment given in mild forms includes oral hydration using solutions with electrolytes, use of antipyretics if necessary, breastfeeding; In the case of patients with warning signs, early and adequate replacement with isotonic solutions has been shown to modify the course and severity of the disease.

Given the clinical suspicion of dengue infection in pregnant women, especially in inhabitants of endemic areas, importance should be given to monitoring newborns and being attentive to the clinical variations that they present due to the initial nonspecificity of symptoms and their subsequent complications. which may include bleeding or shock.

Surveillance, monitoring and timely treatment is of vital importance.

If a woman contracts dengue during pregnancy, doctors should consider the possibility of vertical transmission, treat the mother, and monitor for possible vertical transmission.

During late pregnancy, women living in endemic areas should consider using preventive measures, such as increased vigilance to avoid mosquito bites, to reduce the risk of infection.

From a pathophysiogenic point of view, it is

hypothesized that maternal dengue antibodies play a dual role: first they protect and then increase the risk of developing dengue hemorrhagic fever/dengue shock syndrome in infants who become infected with the virus of dengue 2.

TRANSMISSION BY SEXUAL CONTACT

At the end of September 2019, two cases of dengue were confirmed in men residing in the municipality of Madrid, in which epidemiological and microbiological investigations determined that one was an imported case and the other was autochthonous, the transmission of which had occurred by sexually. The latter was a 36-year-old man who had not left Spain in the 45 days prior to the onset of symptoms, therefore being a native case.

Since September 15, he had fever, headache, back pain, myalgia, diarrhea and rash.

His partner, a 41-year-old man, had presented a very similar clinical picture with the onset of symptoms on September 5.

His history was a trip to Cuba and the Dominican Republic during his incubation period, which is why he was considered an imported case.

Both cases were diagnosed by PCR in serum and urine, respectively, and subsequently confirmed by the laboratory of the National Center for Microbiology.

The entomological investigations did not detect the presence of *Aedes* either in the place of residence or in any of the places visited by the cases in the Community of Madrid.

The cases had unprotected sexual relations in the 3 days following the onset of the imported case's symptoms, so semen samples were requested from the patient, which were positive for dengue virus.

Genetic sequencing confirmed that the virus strain in both cases was identical and coincided with that identified in cases recently imported from Cuba and also analyzed at the CNM.

In the absence of data supporting a possible vector transmission, the sexual route has been considered the most probable in this case.

Although sexual transmission of dengue is theoretically possible and is demonstrated for other similar viruses belonging to the same family (such as the Zika virus), the appearance of more cases associated with this route of transmission cannot be ruled out, as well as the existence of previous cases that were attributed to vector transmission in endemic or with the presence of mosquito vectors.

The presence of the virus has been detected in both semen and vaginal secretions of patients up to 37 and 18 days, respectively, after the onset of symptoms, respectively, and sexual transmission of the dengue virus is considered possible.

TRANSMISSION DUE TO LABORATORY ACCIDENTS

In Korea, the case of a 30-year-old laboratory worker exposed to the dengue virus by needle prick while filtering the virus has been described.

The laboratory where he worked was a biosafety level 2 research center.

When she was injured by the syringe needle, she was responsible for infecting mosquito cell cultures with the dengue virus type 2 (DENV-2).

While sucking the viral solution into the syringe, she removed the needle attached to the syringe and was injured.

During admission, he presented symptoms of fever, nausea, myalgia, and a characteristic maculopapular rash with elevated aspartate aminotransferase (AST) of 235 IU/L and alanine aminotransferase (ALT) of 269 IU/L.

She had been diagnosed by a positive nonstructural protein 1 (NS1) rapid antigen (Ag) test one day before the onset of symptoms along with a positive immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) in the ninth

day from the onset of symptoms.

TRANSMISSION BY TRANSFUSIONS

A study published in The Journal of Infectious Diseases indicated that during a large dengue epidemic in Sao Paulo (Brazil), people who showed up at different blood centers to donate blood, 0.51% on average, were infected with the virus that causes the disease (DEN) even if they did not exhibit symptoms during the procedure.

The investigation also revealed that 37.5% of the patients who received the contaminated blood bags and were susceptible to the virus (had not been previously infected) contracted dengue, although no severe case of the disease was recorded.

No significant difference was observed in relation to mortality or even the severity of symptoms such as fever, malaise, bleeding or plateletopenia.

At the time when there was a large circulation of DEN serotype 4, all donors were invited to participate in the study and donate an extra blood sample for analysis for viral RNA.

Samples were drawn from 39,134 donors in total.

The result was positive in 0.51% of cases.

Blood bags contaminated with DEN-4 were transfused to 22 recipients.

Of these, only 16 were susceptible to the disease, as they did not have markers of recent DEN-4 infection.

In the end, six people were effectively infected, resulting in a transfusion transmission rate of 37.5%.

In Brazil, the current routine of blood banks includes tests for the detection of AIDS, hepatitis C, hepatitis B, human T-cell lymphotropic virus (HTLV), syphilis and Chagas disease.

Arboviruses, such as those that cause dengue, Zika and chikungunya, can currently only be detected with PCR-type molecular tests, which are more expensive than serological tests, intended for the search for antibodies.

Transfusion-transmitted cases can also cause

symptomatic disease; That is why effective prevention measures must be implemented, at least in the cases of a fraction of the most vulnerable donors.

Recently, the Ministry of Public Health of Salta (Argentina) informed the community of important aspects to take into account when donating blood, in the case of having had dengue or having received the vaccine against the disease.

In this regard, it was explained that every donor, first of all, goes through an interview, in which they are questioned about whether they present symptoms compatible with dengue, Zika or chikungunya.

Once the donation has been made, the donor is provided with the Institution's telephone number, so that they can report within 24 to 48 hours, in the event that symptoms appear, in order to discard the blood.

If the person has a diagnosis of dengue, they will be able to donate three months after receiving a medical discharge.

If the potential donor or a living family member has symptoms of dengue, they must wait for 4 weeks to complete the donation.

TRANSMISSION BY TRANSPLANTS

Non-vector forms of transmission of dengue can occur through organ transplantation.

In one study, the medical records of donors and recipients with suspected dengue in the first week post-transplant were reviewed.

They used serological and molecular analyzes to confirm the infection, which made it possible to detect four cases of dengue virus transmission through solid organ transplantation.

The recipients had positive serology and RT-PCR.

Infection in donors was detected by serology.

All cases presented fever within the first week after transplant.

There were no fatal cases.

After these cases, dengue screening with detection of the NS1 antigen in donors during dengue outbreaks was implemented at the

reference center and no new cases were detected.

In endemic regions, it is important to suspect and detect dengue in febrile and thrombocytopenic recipients in the postoperative period.

There is no strong recommendation for screening donors for dengue in transplant guidelines, but in endemic areas, physicians should be aware of this type of transmission before transplant.

Unforeseen transmission of an infectious disease from an organ donor to a recipient is a rare event; however, when it occurs, it is associated with significant morbidity and mortality.

Therefore, the goal of organ donation and transplantation programs is to minimize such events while maximizing transplant opportunities.

This goal is based on (i) rational donor screening policies based on an understanding of the epidemiology of the infectious diseases of interest and the performance characteristics of the tests used to diagnose them, and (ii) evidence on patient outcomes. In case of disease transmission, to facilitate informed decision making regarding the risk trade-off between accepting an organ with a higher risk of disease transmission versus remaining on the waiting list.

CONCLUSIONS:

This literature review summarizes case reports, peer-reviewed literature, and international guidelines.

Through it, we objectify that the non-vector transmission of dengue is a confirmed and unavoidable fact.

Despite its low incidence, it must be taken into account that it will increase during epidemic periods, and that an accurate diagnosis can only be made when the possibility of contagion beyond the mosquito bite is kept in mind.

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