DENGUE VIRUS INFECTION DURING PREGNANCY: A SYSTEMATIC REVIEW

INFECCIÓN POR EL VIRUS DEL DENGUE DURANTE EL EMBARAZO: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

INTRODUCTION: Every year, dengue in Tamaulipas seriously affects pregnant women, increasing complications such as preeclampsia, hemorrhage, shock, premature births and low neonatal weight. On this matter, prevention, early recognition and an accurate diagnosis of dengue are crucial to reduce or regulate possible complications that can arise in these patients.

OBJECTIVES: To update and establish epidemiological data, diagnostic criteria, treatments and preventive measures for dengue, focusing on vulnerable groups (mainly pregnant women) and future alternatives for its management.

MATERIALS AND METHODS: Databases such as PubMed, Google Scholar and ScienceDirect were used to obtain articles with a publication date no older than 5 years as inclusion criteria. After screening and collaborative evaluation, 16 relevant publications focused on dengue were selected, prioritizing those that emphasized in the relationship between pregnancy and dengue.

RESULTS: Data was analyzed and established about epidemiology, vectors and control measures, pathophysiology, types of infections and classification, clinical manifestations, involvement during pregnancy, diagnosis and treatment of dengue.

CONCLUSIONS: Although pregnancy does not increase the risk of dengue, facing the disease during pregnancy can cause serious maternal and neonatal complications. Currently, due to the absence of an antiviral treatment, preventive measures are essential in Mexico and in the rest of the world.

KEYWORDS: Dengue; vector borne disease; pregnancy; preeclampsia; shock.

RESUMEN

INTRODUCCIÓN: Cada año, el dengue en Tamaulipas afecta gravemente a las mujeres embarazadas, incrementando complicaciones como preeclampsia, hemorragia, shock, partos prematuros y bajo peso neonatal. Al respecto, la prevención, el reconocimiento temprano y el diagnóstico certero del dengue son cruciales para reducir o regular las posibles complicaciones que pueden presentarse en estas pacientes.

OBJETIVOS: Actualizar y establecer datos epidemiológicos, criterios diagnósticos, tratamientos y medidas preventivas del dengue, centrándose en los grupos vulnerables (principalmente embarazadas) y alternativas futuras para su manejo.

MATERIAL Y MÉTODOS: Se utilizaron bases de datos como PubMed, Google Académico y ScienceDirect para obtener artículos con fecha de publicación no mayor a cinco años como criterio de inclusión. Tras la depuración y evaluación colaborativa, se seleccionaron 16 publicaciones relevantes centradas en dengue, priorizando aquellas que enfatizaban en la relación entre embarazo y dengue.

RESULTADOS: Se analizaron y establecieron datos sobre epidemiología, vectores y medidas de control, fisiopatología, tipos de infecciones y clasificación, manifestaciones clínicas, afectación durante el embarazo, diagnóstico y tratamiento del dengue.

CONCLUSIONES: Aunque el embarazo no aumenta el riesgo de dengue, enfrentar la enfermedad durante la gestación puede causar complicaciones maternas y neonatales graves. Actualmente, debido a la ausencia de un tratamiento antiviral, las medidas preventivas son esenciales en México y en el resto del mundo.

PALABRAS CLAVE: Dengue; enfermedad transmitida por vectores; embarazo; preeclampsia; shock.

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PROBLEM STATEMENT

Due to the increase in cases of dengue virus infection (reported by the World Health Organization [WHO] in 2023), it is pertinent to conduct a literature research with updated epidemiological data on the geographical distribution of the disease, mainly in our area, as well as prevention and treatment measures in vulnerable groups of the population, mainly pregnant women, since it can result in labor and postpartum complications, and be the cause of devastating consequences on both the mother and the product.

OBJECTIVES

Collect updated epidemiological data on dengue virus distribution.

Establish updated diagnostic criteria for dengue fever.

Inquire into current treatments and possible future alternatives for prevention and treatment of the disease.

Establish preventive measures, mainly for groups vulnerable to developing complications, such as pregnant women.

INTRODUCTION

During 2024, Tamaulipas, a state of Mexico, had an increase in cases of dengue. It is of relevance to mention that pregnant women with dengue possess high risks for presenting complications (such as shock, due to plasma extravasation, severe hemorrhage, and preeclampsia), as well as the existence of the strong relationship between dengue, premature delivery and low birth weight in the product. This motivates the search for information about the current geographical distribution of the virus and its vector, preventive measures (which has importance in risk groups, such as pregnant women), diagnosis and treatment based on current evidence. Also, it is crucial to promote dissemination about this subject in the medical community, emphasizing in preventive measures that are capable of avoiding complications in high risk groups, predominantly pregnant women.

Dengue virus (DENV) is responsible for an arboviral disease (vector-borne disease) transmitted to humans by the bite of mosquitoes from the Aedes genus (*Aedes aegypti, Aedes albopictus*). The serotypes of the Dengue virus are known as DENV-1, DENV-2, DENV-3 and DENV-4, all of which can cause human disease. Its infection may be asymptomatic, a mild febrile illness, or a severe form, which can cause coagulopathy and increase vascular fragility and permeability (dengue hemorrhagic fever). This previous mentioned condition can progress to a hypovolemic shock, known as dengue shock syndrome (DSS).[1]

Some groups of the population, such as pregnant and postpartum women (especially up to 14 days postpartum), are more susceptible to complications and progression to severe forms of dengue.[2] A pregnant woman infected with dengue may present major influences on her health and in the product's health too. Severe dengue poses additional risks to pregnant women due to the possibility of developing preeclampsia, gestational hypertension, hemolysis, organ dysfunction, and even death. Likewise, premature deliveries and low birth weight in newborns are frequently observed, leading to serious effects on the child's health and development. For this reason, an early and accurate diagnosis plus specialized care are important to improve maternal and perinatal outcomes in dengue-infected pregnancies.[3]

The research question on which this systematic review is based is the following: Which risk factors, complications, preventive measures and treatment in pregnant women infected with dengue virus can modify the prognosis of the disease?

MATERIALS AND METHODS

Inclusion criteria: Articles with publication dates no older than 5 years.

Exclusion criteria: Articles that were published in a language other than English or Spanish.

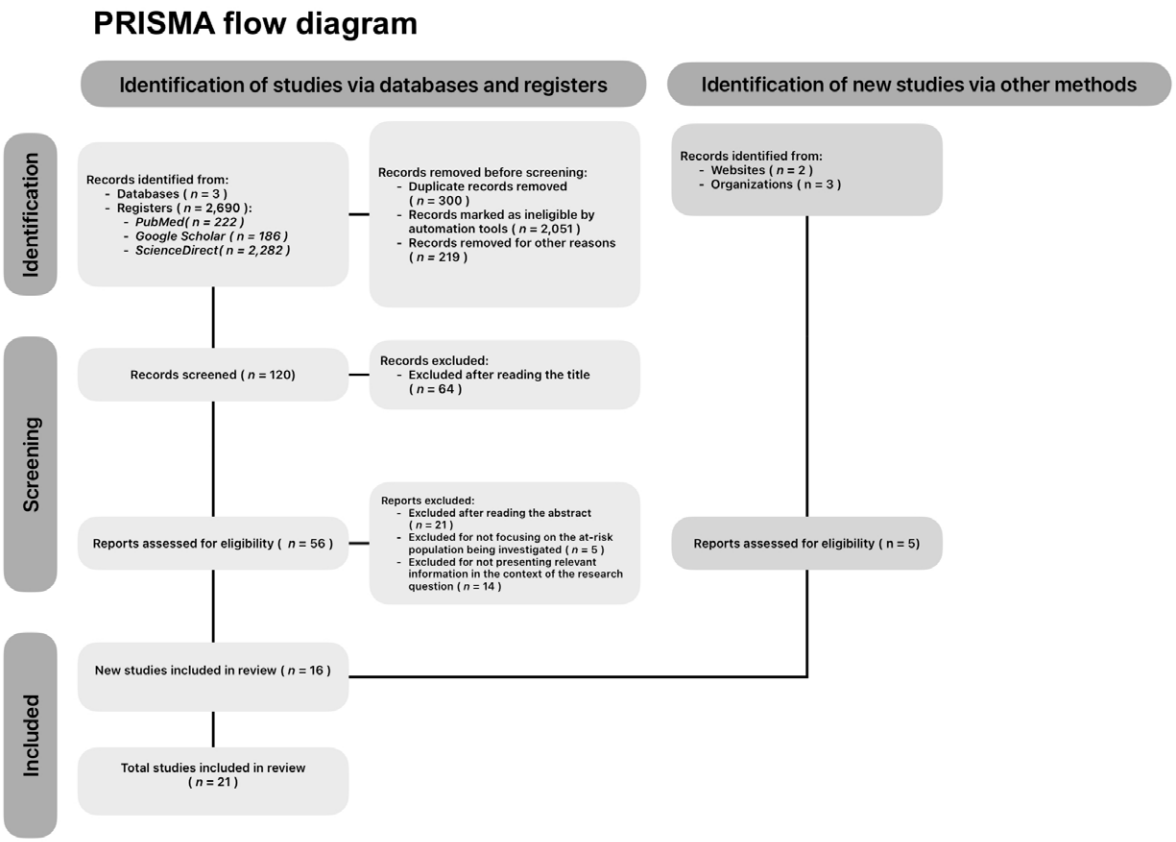
In the PubMed database 222 records were initially identified using the following MeSH and Booleans combinations: ((“Severe Dengue/classification”[Mesh]) OR (“Severe Dengue/diagnosis”[Mesh])) OR (“Severe Dengue/epidemiology”[Mesh] OR “Severe Dengue/physiopathology”[Mesh] OR “Severe Dengue/prevention and control”[Mesh] OR “Severe Dengue/therapy”[Mesh]); in Google Scholar 186 records were initially identified using the same combinations with the specific terms “severe dengue” AND (classification OR diagnosis OR epidemiology OR physiopathology OR prevention OR control OR treatment OR therapy); 2 282 records were initially identified in the advanced search of the ScienceDirect database under the terms “severe dengue” AND (classification OR diagnosis OR epidemiology OR physiopathology OR prevention OR control OR treatment OR therapy).

Subsequently, the initial search was modified by applying the no more than 5 years of publication date filter, discarding duplicate citations and some other reasons at the discretion of the main authors, resulting in 120 post-screening records. Through the reading of the titles and collaboratively discussing the usefulness and relevance for the review, those reports were evaluated individually by the 6 authors, as well as voting on the eligibility of each one of them, concluding with the inclusion of 56 reports.

Afterwards, 3 of the authors read the abstract of the 56 reports previously selected, taking into account those that focused on the population of the PICO question and those who

had relevant information that was related or might answer the initial research question. This ended with the inclusion of 16 reports. Subsequently, the information was compiled by 3 of the authors after a complete reading and synthesis of the 16 reports, focusing on data of the geographic distribution of dengue virus, preventive measures, risk factors, prognosis, diagnosis and treatment in pregnant women. Thereafter, the other 3 authors reviewed the compiled information for its final inclusion, evaluating the level of evidence of the articles from which the information was obtained. Also, the epidemiological bulletin of Tamaulipas and definitions provided by the National Institute of Health (NIH) were used as sources of information to obtain data on the geographic distribution of dengue virus in the state of Tamaulipas. Additionally, 3 citations were employed from the World Health Organization (WHO) and the Centers for Disease Control (CDC) organization for obtaining definitions, clinical manifestations and preventive measures of dengue. These were included at the discretion of the other 3 authors due to their relevance in the development of the research (Image 1).

Image 1. Systematic review flow diagram. The PRISMA flow diagram for the systematic review details the identification of studies for the review via databases and registers, as well as identification of studies via other methods.



DENGUE VIRUS

There are more than 70 major pathogens in the Flaviviridae family that cause disease in human beings; the Dengue virus (DENV) is one of these pathogens belonging to this family and mainly affects tropical regions.[1]

DENV is an arbovirus (arthropod-borne virus) that is transmitted through a vector (mostly *Aedes aegypti*), causing dengue infection, which in a public health perspective is a disease with great relevance.[4] It is an enveloped virus that has an icosahedral capsid that contains 11 kilobases of positive sense ssRNA (single-stranded RNA) that encodes three structural and seven nonstructural proteins. Based on antigenic differences, four serotypes of DENV were identified that share 65 % of their genome. These serotypes are known as DENV-1, DENV-2, DENV-3 and DENV4. Although, a fifth serotype (DENV-5) has recently been identified in Malasyia.[4]

The serotypes cause diverse immune responses by infecting their respective target cells, thus triggering a potent cytokine response that influences disease severity. In ad-

dition, a secondary infection with another serotype may evoke a more rapid and severe immune response due to antibody-dependent enhancement (ADE).[4]

DENGUE PROTEINS

The genome of the DENV is encoded into seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5) and three structural proteins (capsid protein "CP", envelope protein "EP", and membrane protein "MP"). Although, DENV has non-coding regions (NTRs) which are found at the 3' end of the genome.[1]

As their name indicates, the three structural viral proteins give the structure to the DENV, and the NS proteins are responsible of entry of the virus into the target cell, virus replication, assembly, and pathogenesis, leading to the host's disease.[1]

The NS1 protein has multiple intracellular and extracellular functions in the host's target cells; also, this antigen functions as a marker for diagnosing and evaluating the DENV infection in early stages. This protein is involved in the severe pathophysiology of dengue by facilitating plasma leakage. This is achieved by activating Toll-like receptor 4 (TLR4) of macrophages and disrupting endothelial cells, which results in vascular leakage.[5]

NS3 is a protease that needs a cofactor (NS2B) to assist in the virus replication. This protein also modulates the viral infection by interacting with NS4B. NS4A induces autophagy and prevents cell death, which facilitates the process of viral replication.[5]

The NS5 protein has methyltransferase and guanylyltransferase activities that are involved in mRNA protection. This protein is found in infected cells, specifically in their nucleus, which suppresses the host's antiviral response.[5]

On the other hand, the DENV envelope protein (EP) is a structural protein that facilitates the binding process of the virus to the target cell receptor, allowing its entry into the host cell. When the viral genome is synthesized, it associates with the capsid proteins (CP) which forms a nucleocapsid that enters into the endoplasmic reticulum lumen along with the envelope (EP) and membrane (MP) viral structural proteins.[5]

EPIDEMIOLOGY

In recent years, the incidence of dengue has increased exponentially worldwide: the number of cases reported by the WHO has risen from 505 430 in 2000 to 5.2 million in 2019. In most cases, the person is asymptomatic or presents mild symptoms that can be controlled without medical intervention. It is important to mention that there are a large number of cases that are misdiagnosed as other febrile illnesses or aren't reported, which suggests that the actual number of cases should be higher.[6]

The highest number of dengue cases was reported in 2023, affecting more than 80 countries. Since the beginning of 2023, persistent dengue transmission, combined with an unexpected peak in cases, resulted in the reporting of an all-time high of more than 6.5 million cases and more than 7 300 dengue-related deaths.[6]

Currently, the disease is endemic in more than 100 countries in Africa, the Americas, South-East Asia, the Eastern Mediterranean and the Western Pacific. The Americas, South-East Asia and Western Pacific Regions are the most affected, with Asia accounting for about 70 % of the global burden of the disease.[7]

A more than twofold increase in new cases has been reported nationwide in Mexico in the 34th epidemiological week of the year 2024 in comparison to 2023 (Table 1).[7]

Table 1. New cases of dengue in Mexico up to week 52 of 2024. Extracted from the national epidemiological bulletin week 52, 2024 (December 22 to 28, 2024) by the National Epidemiological Surveillance System of Mexico.[7]

Disease	Week 52, 2024	Accumulated total of cases (2024)	Weekly median (2019-2023)	Week 52, 2023	Accumulated total of cases (2023)
Dengue without warning signs	297	68 249	109	552	28 871
Dengue with warning signs	420	52 697	171	513	23 882
Severe dengue	25	4 214	26	44	1 653

According to data provided by the national epidemiological bulletin for week 52, 2024, in Tamaulipas, 1 668 cases of non-severe dengue, 815 cases of dengue with warning signs and 52 cases of severe dengue have been reported.[7]

According to data from SINAVE (the National Epidemiological Surveillance System of Mexico) on the incidence rate of dengue in 2024, measured in cases per 100 000 inhabitants, in Tamaulipas (until epidemiological week 52, which covers from December 23 to December 30) an average of 67.37 cases per 100 000 inhabitants was registered, placing Tamaulipas within the 20 states with the highest incidence rate, but below the total national rate which was 94.60. The municipalities in the metropolitan area of Tamaulipas registered an average of 41.34 cases per 100 000 inhabitants, remaining below the national and state average. Although there is an incidence rate lower than the national average, the data reflect a significant burden of cases, making it important for the state to implement control and prevention mensures.[7]

VECTORS OF DENGUE VIRUS AND THEIR DISTRIBUTION

Worldwide, *Aedes aegypti* is the main vector for DENV and is distributed in tropical regions, while *Aedes albopictus* is a secondary vector in Asia and has also been identified in urban areas of various countries across the USA and Europe, mainly in tropical and temperate regions.[8,1]

Ae. aegypti has the ability to reproduce in natural and artificial habitats, such as tires, water containers and storm drains, which therefore makes it a common vector in urban areas. If kept dry, their eggs may remain latent for months and hatch when they are in contact with water. For that reason, it is highly important to constantly empty water containers to prevent the hatching of *Aedes aegypti* eggs.[8]

During the day, this vector feeds primarily on human blood and has indoor resting behavior (bedrooms, living rooms, bathrooms, etc.). The main factors that contribute to the presence and population size of these vectors are a 25-30 °C temperature (which is the optimum range for their development, when it exceeds 40 °C or is below 10 °C, mosquitoes die, and eggs and larvae stop developing), rainfall and humidity.[1]

VECTOR CONTROL MEASURES

In 2009, The World Health Organization (WHO) established 4 main approaches with the objective of controlling and inhibiting the spread of the dengue vector:

1. Chemical control (such as insecticides which reduce mosquito populations, including space spraying, residual spraying, application of larvicides, etc).[9]

2. Biological control (such as fish, copepods, *Bacillus thuringiensis israelensis* and *Wolbachia*, all of which reduce and control mosquito populations).[9]

3. Vector source reduction (community outreach is necessary, which has the objective of promoting the elimination or reduction of mosquito breeding sites, such as water containers, storm drains, tires, etc.).[9]

4. Personal or barrier protection (such as the implementation of mosquito nets at home, repellents, or protective clothing).[9]

PATHOPHYSIOLOGY

During mosquito blood-feeding in humans, DENV apparently injects into the bloodstream, spilling into the epidermis and dermis, leading to infection of Langerhans cells (DCs of the epidermis) and keratinocytes.[10]

Post-infection, infected cells migrate from the initial site of infection to lymph nodes. Monocytes and macrophages are attracted to the lymph nodes and thus become susceptible to infection.[10] This promotes infection and spreads the virus throughout the lymphatic system. The term "viremia" refers to the initial phase of viral infection, during which the virus enters the bloodstream and begins to spread. This stage involves infection of numerous mononuclear cells, including bloodstream monocytes, myeloid DCs and macrophages in the spleen and liver.[10]

During the initial viral infection in dengue, the virus spreads rapidly through the host circulatory system, resulting in systemic dissemination. This phase is very important for the establishment of infection because the virus gains access to many tissues and organs, allowing further replication and amplification.[10]

Infected mononuclear cells, especially dendritic cells and macrophages, play an important role in the virus reaching lymphoid organs, where it can evade the host immune response and spread.[10]

The intensity and duration of initial viremia are major predictors of disease severity and can impact the clinical outcomes of dengue patients. This stage must be effectively managed to control the spread and progression of the infection.[10]

SECONDARY DENGUE INFECTION

Even though primary infection confers long-lasting, if not lifelong, protection against reinfection by a homologous serotype of DENV, secondary infection by a heterologous

serotype of DENV occurs frequently in endemic areas and is established as the most important risk factor for severe disease.[11]

In secondary infection the antibodies produced during the initial infection by DENV bind to the different DENV serotypes, but do not neutralize them. It has been proposed that the binding of an antibody to a virus of a different serotype allows cells, such as macrophages and monocytes, to potentially take up more viruses, leading to increased virus production, viremia, and pathogenesis.[10]

These antibodies allow the virus to enter cells with Fcγ receptors (FcγR), which increases viral levels and worsens the disease. In addition, FcγR-mediated DENV infection effectively suppresses the host innate antiviral immune response, leading to increased intracellular replication.[10]

CLINICAL PRESENTATION

The incubation period of dengue varies between 5 to 7 days and has an abrupt onset. The course of the disease follows 3 phases: febrile, critical and convalescent.[12] (Table 2).

Table 2. Course of dengue[13]

Febrile phase	Usually lasts one week (2-7 days). Clinical manifestations: - Fever - Headache - Retroocular pain - Myalgias and arthralgias - Macular or maculopapular rash - Vomiting - Minor hemorrhagic manifestations including petechiae, ecchymosis, purpura, epistaxis, gingival bleeding, hematuria or a positive tourniquet test result.
Critical phase	Life-threatening phase due to the appearance of manifestations such as plasma leakage and internal bleeding.
Convalescent phase	Recovery of vascular patency and reduction of signs and symptoms.

Dengue virus infection may be asymptomatic or cause a mild febrile illness, but if it becomes severe, it can cause coagulopathy, increased vascular fragility and increased permeability. Such a condition is called dengue hemorrhagic fever, which can progress to hypovolemic shock, known as dengue shock syndrome (DSS).[1]

Studies have shown that pre-existing factors such as diabetes, hypertension, renal disease, cardiovascular disease and the occurrence of vomiting, abdominal pain and tenderness, bleeding or fluid accumulation during the febrile phase of illness have been associated with progression to severe disease. Other factors that have also been associated with severe illness during the febrile phase include DENV-2 infection in children, secondary infection, low platelet count, low serum albumin, and high AST and ALT enzyme concentrations.[14]

WHO 2009 DENGUE CLASSIFICATION

Dengue

Dengue is defined by the presence of ≥2 clinical findings (nausea, vomiting, rash, joint or muscular pain, a positive tourniquet test, leukopenia, or any warning signs) in a febrile person who lives in or has traveled (within the past 14 days) to a dengue-endemic area.[12]

Dengue with warning signs

Is defined as dengue with presence of abdominal pain or tenderness, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, restlessness, and hepatomegaly. Patients with warning signs should be monitored, as they are more likely to progress to severe disease.[12]

Severe dengue

Is defined as Dengue with presence of severe plasma

leakage resulting in shock or fluid accumulation along with respiratory distress, severe bleeding, or severe organ failure such as hepatitis (elevated transaminases ≥1000 IU/L), altered consciousness, or heart failure.[12]

DENGUE FEVER DURING PREGNANCY

An association has been found between dengue virus infection in pregnant women and adverse outcomes such as maternal mortality, fetal death, and neonatal mortality. Therefore, it is imperative that pregnant women be considered a population at risk for dengue management programs.[15]

Vertical transmission is possible if the mother presents clinical manifestations of dengue in late pregnancy or even during delivery. Newborns may be asymptomatic (in majority) or can develop symptoms within 14 days after birth (commonly within the first week). Clinical presentation in infants varies from common mild dengue symptoms to severe dengue with shock and hemorrhagic manifestations.[16]

DIAGNOSIS

The procedures used to diagnose DENV infections in pregnant and postpartum women are the same as those used in the rest of the population. Nevertheless, it is important to mention that, in pregnant women, some of the clinical manifestations of the disease can be confused with common manifestations such as nausea, vomiting, abdominal pain, postural hypotension and tachycardia, which delays diagnosis and early hydration measures.[2]

Diagnosis can be made by detection of viral components (antigens) in the blood or by serological tests (antibodies). The choice of test depends on the day on which clinical manifestations began to appear.[17]

Antigen detection:

- During the early stages of the disease, in the febrile phase, detection of viral components in the circulation is very sensitive. Viral nucleic acid in serum can be detected by reverse transcriptase polymerase chain reaction (RT-PCR) or by detection of virus-expressed soluble nonstructural protein 1 (NS1) by enzyme-linked immunosorbent assay (ELISA).[17]

- NS1 antigen can be detected from day 0 onwards, with a slightly peak on the fourth day. Its detection is not affected by the presence of IgM, which occurs from day 3 to day 9 of infection.[13]

Antibody detection:

- The detection of IgM and IgG can be performed by serological tests from the third or fifth day of illness. It is also useful to distinguish between primary or secondary dengue infections.[17]

- From the third or fourth day after the onset of symptoms, IgM detection can be performed and on the fifth day, it will reach a persistent amount in the serum.[17]

- Effective detection of IgG is only possible from day 10 or 15 after the onset of symptoms. IgG detection assays are useful to differentiate between primary and secondary infection, since after the onset of symptoms during a secondary infection, IgG is detectable from day 3 due to the rapid immune memory response.[13]

TREATMENT

The patient can be classified into three groups: Group A (outpatient treatment), Group B (observation or hospital admission), and Group C (emergency department/intensive care). Dengue is a disease with a dynamic evolution, which allows the patient to be reclassified according to reevaluations.[18]

In group A, the patient has no comorbidities and presents clinical manifestations of dengue without warning signs and should be treated with hydration and oral symptomatic treatment at home. It should be recommended to return to the health unit daily for re-evaluation to determine hematocrit and platelet count, especially when fever ceases at the end of the acute phase.[18]

In group B, the patient should receive rehydration with medical supervision or hospitalization if there are warning signs. If during re-evaluation the patient has stable hemogram and hematocrit, hemodynamic stability and absence of warning signs, the patient can be discharged and continue treatment as group A. Group B patients with warning signs require hospitalization for a minimum of 48 hours. Intravenous hydration should be started immediately with an isotonic solution (saline or Ringer's lactate) and follow-up (clinical and laboratory) every two hours. If the patient in question evolves with hemodynamic stability, with preserved diuresis and decrease in hematocrit, the patient can move on to the maintenance phase. If the patient does not improve after two hours, rehydration should be repeated up to three times, and if the response is unsatisfactory, the patient should be reclassified into group C (severe shock).[18]

An individual infected with DENV and classified as group C should receive intravenous hydration with isotonic fluids and be admitted to an intensive care unit (resuscitation with isotonic crystalloids). After fluid replacement, a new clinical and hematocrit evaluation is performed. If there is a favorable clinical response, the patient is classified in group B; if ins-

tability persists, colloid (albumin) infusion or blood transfusion is evaluated if there is evidence of hemorrhage indicated by a lack of response or a drop in hematocrit.[18]

In the absence of response to resuscitative therapy and a drop in hematocrit, the possibility of occult bleeding should be ruled out, evaluating the indication for blood transfusion and investigating the existence of any organ compromise such as congestive heart failure. Hospital discharge should be considered when the following clinical and laboratory criteria are met: hemodynamic stability and hematocrit, absence of fever in the last 48 hours, platelet count above 50 thousand/ml and absence of signs of secondary infection.[18]

Fever and pain control is preferably done by oral symptomatic therapy, avoiding salicylates and non-steroidal anti-inflammatory drugs (NSAIDs) due to the risk of bleeding. Paracetamol should be administered in the usual doses, six hours apart and a maximum of 4 g/day due to the risk of hepatotoxicity. Fever control in children uses cold/warm compresses. Persistent fever in the acute phase may be a consequence of high viremia and an indicator of severity.[18]

DISCUSSION

Despite efforts to reduce the incidence of cases, dengue continues to be a public health problem in Mexico. The infection may be asymptomatic or cause various clinical manifestations, which may or may not be severe.[19]

Dengue hemorrhagic fever during pregnancy requires specialized management and surveillance. During pregnancy, physiological changes occur in the cardiovascular, respiratory and hematologic system; by the end of the third trimester, plasma volume increases by approximately 40 %, resulting in dilutional anemia which can mask the hemoconcentration of dengue hemorrhagic fever, leading to delayed diagnosis and treatment, mainly in patients with severe blood volume deficiency. Plasma leakage accumulates in the interstitial space of the tissue and causes inadequate tissue oxygenation. Prolonged impairment may progress to multi-organ failure and rapid fetal death, especially in the obstetric population, where oxygen consumption is twice as high as in healthy adults.[19]

The manifestations of severe dengue (such as thrombocytopenia and elevated liver enzymes) overlap with specific pregnancy diseases such as preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) or gestational thrombocytopenia. It has been reported that dengue may be associated with a maternal mortality of up to 15.9 %. Severe dengue infection was associated with increased postpartum hemorrhage. Therefore, the severity of infection may have a significant influence on maternal complications. The risk of vertical transmission is estimated at 18.5 % and 22.7-56.2 % when maternal infection occurs 15 days before delivery and up to two days after delivery.[20]

Early identification of dengue and its appropriate care are associated with a decrease in mortality during pregnancy. The management of acute dengue infection in pregnant women is similar to that of non-pregnant patients and consists of supportive measures (essentially fluid replacement and analgesia). However, pregnant women belong to the group of dengue associated with some conditions of vulnerability according to the WHO/PAHO classification of dengue and, therefore, should be monitored as if they were hospitalized. When labor begins, the pregnant woman should be transferred to a tertiary center capable of handling obstetric hemorrhage as a preventive measure in case it occurs. Organ dysfunction in pregnant women with dengue requires particular vigilance and management in intensive care units.[20] It is important to mention that treatment of obstetric patients consists of fluid administration and transfusion of blood products in case of hemorrhage. Therefore, a plan for rapid and timely administration of blood products should be implemented before delivery in order to provide the greatest benefit to the mother and her child.[19]

Limitations: The main limitation of this review is that several of the included studies were systematic reviews, which means that a low methodological quality or biases, such as selection biases, could have influenced the reliability of their conclusions. Another limitation was the availability and accessibility of various studies, due to the fact that many that seemed relevant to the review had access barriers, such as foreign languages, visualization costs, etc. Also, there is a wide heterogeneity in the included studies, as they are very diverse in terms of population, interventions and designs, which hindered the task of synthesis.

CONCLUSION

Pregnancy does not increase the risk of contracting dengue; however, the disease can have devastating consequences at this stage for both the mother and the product. Although pregnant women represent a particular risk group for possible complications associated with dengue infection (such as shock due to plasma extravasation, severe hemorrhage, preeclampsia, etc.), it is important to mention that there is a strong relationship between dengue, preterm delivery and low weight at birth. Since there is currently no effective antiviral treatment for patients with dengue and the treatment is based on symptoms (only for control purposes), it is of utmost importance to take preventive measures to reduce the incidence of cases of this public health problem that nowadays is present in Mexico and in the rest of the world.[19]

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