

## Original Research Article

**Literature Review: Impact of Dengue Fever on Pregnancy****Ni Putu Savitriyani<sup>1</sup>, Kartika Ishartadiati<sup>2</sup>, Andra Agnez Al Aska<sup>3</sup>, Sukma Sahadewa<sup>4</sup>**Medical Education, Faculty of Medicine, University of Wijaya Kusuma Surabaya<sup>1</sup>Department of Parasitology, Faculty of Medicine, University of Wijaya Kusuma Surabaya<sup>2</sup>Department of Parasitology, Faculty of Medicine, University of Wijaya Kusuma Surabaya<sup>3</sup>Department of Public Health Science, Faculty of Medicine, University of Wijaya Kusuma  
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email : [savitriyaniputu66@gmail.com](mailto:savitriyaniputu66@gmail.com)**ABSTRAK**

Demam berdarah dengue (DBD) atau yang sering dikenal juga dengan dengue hemorrhagic fever merupakan suatu penyakit infeksi akut yang dapat disebabkan oleh virus dengue. Tujuan penelitian ini untuk mengetahui pengaruh demam berdarah dengue (DBD) pada kehamilan. Penelitian ini adalah literature review dengan artikel yang digunakan berasal dari Pubmed dan Google Scholar, yang dipublikasikan pada tahun 2012-2022 dengan populasinya adalah ibu hamil. Hasil pencarian diperoleh 9 artikel yang sesuai dengan kriteria inklusi, kemudian artikel direview. Hasil review menunjukkan bahwa pengaruh demam berdarah dengue pada kehamilan yaitu kelahiran premature, berat badan lahir rendah, dan bayi lahir mati.

**Kata Kunci: Demam berdarah, kehamilan.****Abstract**

*Dengue hemorrhagic fever is an acute infectious disease that can be caused by dengue virus. This study aimed to determine the effect of dengue hemorrhagic fever (DHF) on pregnancy. This research is a literature review with articles used from Pubmed and Google Scholar, published in 2012-2022 with the population being pregnant women. The search results obtained 9 articles that fit the inclusion criteria, then the articles were reviewed. The review results showed that dengue hemorrhagic fever's effect on pregnancy is premature birth, low birth weight, and stillbirth.*

**Keywords: Dengue fever, pregnancy.**

## INTRODUCTION

DHF is a health problem whose number and spread are increasing from year to year which often attacks children (Irma and Masluhiya, 2021). Dengue virus infections worldwide are estimated at 390 million annually (Bhatt et al., 2013). The number of dengue cases has increased more than eightfold over the past 20 years reported to WHO, from 505,430 in 2000 to 2.4 million in 2010 and 5.2 million in 2019 (WHO, 2022). Since January 2022, there have been 87,501 confirmed cases of dengue fever and 816 deaths, according to the Infectious Disease Prevention and Control Agency (P2PM) in Jakarta (Kemenkes, 2022).

This dengue virus infection (DENV) occurs in all age groups, including pregnant women and newborns (Charlier et al., 2017). Dengue fever during pregnancy can have a negative impact on the mother and her fetus, with a maternal mortality rate of 15.9%, this figure is in the high category (Brar et al., 2021). DHF is an acute disease caused by dengue virus infection, clinically DHF manifests as bleeding that can cause shock and death. This dengue fever can be caused by one of four viral serotypes of the genus *Flaviviridae* (Asep, 2014).

When the virus enters the human body through mosquito bites, the virus will enter the lymph nodes through the lymphatic vessels, replicate in the lymph nodes, and then viremia will occur (Silesky-Jiménez & Hidalgo, 2021). The clinical manifestations are as follows: (a) acute fever of sudden onset duration of 2 to 7 days; (b) spontaneous hemorrhagic manifestations or a positive tourniquet test; (c) hepatomegaly; and (d) circulatory failure (Karyanti et al., 2014).

Pregnancy is the union of a man's sperm with a woman's egg. The gestation period is calculated from conception to the birth of the fetus. Normally pregnancy lasts for 280 days (40 weeks or 9 months 7 days) from the date of the last menstruation (Delima, Moidaliza, & Susanti, 2015). Gestational age is classified into 3 categories: premature (<28 weeks), Aterm pregnancy (>37-41 weeks), and post-term pregnancy (>42 weeks) (Putri, Titisari and Setyarini, 2017).

## MATERIAL AND METHODS

Descriptive research with research design is a Literature review that uses data from journals in Pubmed or Google Scholar.

**RESULT**

Table I.1

No	Title and Author	Sample / Sample Size	Subject Characteristics	Result
1.	Spectrum of Mat-ernofetal Out-comes during Dengue Infection in Pregnancy: An Insight (Sharma, <i>et al.</i> , 2016).	The sample is 60 pregnant women. Of the 60 pregnant women, 16 were positive for DHF.	All pregnant women were diagnosed using NS1Ag and/or IgM serology.	The result is that there are 43% of cases are oligohydramnios. Hemorrhagic manifestations occurred in seven women and there were three maternal deaths. For perinatal complications, there was one newborn death.
2.	Symptomatic dengue infection during pregnancy and live birth outcomes in Brazil, 2007-13: A retrospective observational cohort study (Nascimento, <i>et al.</i> , 2017).	The sample was 3898 pregnant women who were confirmed positive for DHF.	Pregnant women with positive DHF and babies born alive.	Dengue infection in pregnant women is associated with an increase in the incidence of premature birth with OR: 1, 26, and p=0.006.
3.	Dengue infection during pregnancy and adverse maternal, fetal, and infant health outcomes in Rio Branco, Acre State, Brazil, 2007-2012 (Feitoza, <i>et al.</i> , 2017).	Two hundred pregnant women were exposed to the dengue virus during pregnancy by random sampling technique.	Dengue-infected pregnant women.	Pregnant women exposed to DHF show an RR: of 3.4 (95% CI: 1.02-11.23) for newborn death.

<p>4. Symptomatic dengue infection during pregnancy and the risk of stillbirth in Brazil, 2006–12: a matched case-control study (Paixão, <i>et al.</i>, 2017).</p>	<p>The samples used were: 275 women who gave birth to stillbirths and 1507 women who gave birth to live babies who were diagnosed with dengue infection during pregnancy.</p>	<p>All pregnancies ending in stillbirths and a random sample of live births between 1 January 2006 and 31 December 2012</p>	<p>Symptomatic dengue infection during pregnancy is almost twice as likely to result in fetal death with OR: 1.9, 95% CI 1.6–2.2.</p>
<p>5. A study of dengue fever in pregnancy and its maternal and fetal prognosis (Gehlot, <i>et al.</i>, 2017).</p>	<p>This study was conducted on 25 pregnant women who were diagnosed and serologically confirmed to have dengue fever.</p>	<p>All pregnant women with fever and serologically confirmed dengue fever.</p>	<p>In pregnant women infected with dengue hemorrhagic fever the results are: spontaneous abortion (4%); premature birth (16%), oligohydramnios (8%) and antepartum hemorrhage (4%).</p>
<p>6. Need for guidelines for the combined management of pregnancy and dengue: a retrospective study from an Indian tertiary care maternity hospital (Kallur, <i>et al.</i>, 2018).</p>	<p>The sample is 44 pregnant women who have a definite diagnosis of dengue fever.</p>	<p>Pregnant women infected with dengue fever. Which is classified into 3 trimesters.</p>	<p>The results obtained in this study were: one stillborn baby, with 45.4% preterm labor.</p>
<p>7. Dengue infection during pregnancy in Burkina Faso: a cross-sectional study (Sondo, <i>et al.</i>, 2019).</p>	<p>The sample consisted of 25 pregnant women who were treated for DHF.</p>	<p>Pregnant women infected with dengue virus who are between 25 and 35 years of age.</p>	<p>The results of the study on DENV-infected mothers showed that: 5 (20%) mothers experienced postpartum hemorrhage. While</p>

				complications to the fetus were: 3 cases of acute fetal distress (12%), and 4 cases of newborn death (44.5%).
8.	Maternal and fetal outcomes of dengue fever in pregnancy: a large prospective and descriptive observational study (Brar, <i>et al.</i> , 2021).	The sample used was 44 pregnant women with DHF.	The research subjects were pregnant women who were diagnosed with DHF in the 1st, 2nd, and 3rd trimesters.	A total of 15 (34.1%) babies were born prematurely and babies with low birth weight, namely 13 (29.5%).
9.	Maternal & perinatal outcome of fever in pregnancy in the context of dengue A retrospective observational study (Sagili, H, <i>et al.</i> , 2022)	55 pregnant women with dengue infection (positive dengue) and 220 pregnant women without dengue fever.	Women who experience fever during pregnancy and undergo dengue infection checks from January 2015 to December 2018.	The result is that there were six maternal deaths due to complications of dengue infection. The risk of stillbirth was 2.67 [95% CI 1.09, 6.57], while LBW [RR : 1.13, 95% CI 0.87, 1.45] and premature birth (RR : 1, 33, 95% CI 0.89, 1.97).

**DISCUSSION**

The table above shows a comparison of research results regarding the effects of dengue hemorrhagic fever on pregnancy, namely premature birth, low birth weight, and stillbirth.

Research conducted by Brar, *et al.* (2021) showed that a total of 15 (34.1%) babies were born prematurely and 13 (29.5%) babies with low birth weight. This is supported by research from Nascimento, *et al.*, (2017) using the cohort study method which shows that the risk of preterm birth increases by 1.26 higher in women with symptoms of dengue infection during pregnancy and this is evidenced by an OR value of 1.26, and a p-value of 0.006.

The association between preterm birth and dengue virus infection in pregnant women is biologically plausible, as the intense inflammatory reaction triggered by maternal infection may indirectly stimulate uterine contractions leading to preterm birth. However, there is a study showing that dengue infection in pregnant women does not increase the risk of adverse fetal outcomes, including miscarriage and preterm birth (Xiong, *et al.*, 2017).

Research conducted by Sagili, H, et al., (2022) in Brazil with the cohort study method showed the results of LBW [RR: 1.13, 95% CI 0.87, 1.45] in women exposed to dengue hemorrhagic fever during pregnancy which means that DHF in pregnancy has a higher chance of causing LBW by 1.13. This is also in line with other studies where infants born to mothers with acute dengue infection experience LBW. LBW can be caused by shorter duration of pregnancy rather than fetal growth disorders in the uterus (Naz, et al., 2022).

Dengue hemorrhagic fever in pregnancy can also result in death in newborns. This is in line with research by Feitoza, et al., (2017) conducted on two hundred pregnant women affected by dengue virus in pregnancy with random sampling technique showed the results of RR: 3.4 (95% CI: 1.02-11.23) for newborn mortality. This is supported by the research of Kallur, et al., (2018) showing the results of: one stillborn baby.

Dependent enhancement (ADE) is a mechanism by which viral replication becomes easier and more widespread. The number of viruses produced becomes more. Immunoglobulin G in infants transmitted from the mother through the placenta will directly bind to dengue viruses of different serotypes and will mediate the endocytosis of the virus into dendritic cells. When the virus enters the dendritic cells, it will interact with Ig-like receptor B1 which has an inhibitory effect on FcR signaling to produce specific antibodies that are more competent to eradicate the virus. In the end, it makes it easier and easier for the virus to replicate freely and further infect other cells. With this ADE mechanism, the number of viruses produced and cells infected will also be greater. So that there is a cell resistance reaction that will produce more inflammatory mediators as well (Handayani, et al., 2017). Inflammatory mediators such as cytokines and chemokines released during dengue fever can trigger premature birth, and LBW (Friedman, et al., 2014).

Cognitive development may be slower in low birth-weight infants than in normal birth-weight infants. LBW can be caused by short gestational age (premature birth), and IUGR (Intra Uterine Growth Restriction). Both causes are influenced by risk factors such as maternal, placental, fetal, and environmental factors. These risk factors contribute to nutritional deficiencies in the fetus during pregnancy (Ismayanah, Nurfaizah, and Syatirah, 2020).

The dengue virus causes mild illness in most infected individuals. In most cases, the illness is characterized by fever, headache, pain behind the eyes, muscle pain, joint pain, vomiting, and diarrhea. A small percentage of patients may experience symptoms such as bleeding, plasma leakage, and thrombocytopenia. Clinical manifestations such as thrombocytopenia, and plasma leakage can interfere with placental circulation, and cause hypoxia with consequences for the fetus in the form of growth retardation and fetal death (Rathore, et al., 2022).

## CONCLUSION

Based on the results of a literature study regarding the effect of dengue hemorrhagic fever on pregnancy in infants and fetuses it can cause premature birth, stillbirth, and low birth weight babies.

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