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AN LITERATURE REVIEW OF DENGUE FEVER: DENGUE HAEMORRHAGIC FEVER IS MORE DEADLY THAN DENGUE FEVER.

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REVIEW ARTICLE

ABSTRACT

Introduction: *800 years ago, dengue developed in monkeys and spread to humans. Up until the middle of the 20th century, the first epidemiological outbreak of dengue occurred in North America, Africa, and Asia in the 1780s. Earlier in 1970, only 9 countries experienced severe dengue epidemics. Perhaps, now that dengue fever occurs in more than 100 countries, the disease is considered endemic.* ***Materials and method:*** *In this study, four articles have been examined, and the majority of the articles focus on the planning and execution of studies, data analysis, and the definition of concepts.* ***Result:*** *In this study, describe DHF changes. The majority of DHF patients are usually infected with two types of serotypes, and among all the DHF patients, adolescents carried a higher percentage compared to young adults and children, and among adolescents, males had a higher percentage compared to females.* ***Conclusion:*** *This study review on dengue hemorrhagic fever shows that it causes severe illness and can even cause death if left untreated.*

Keywords: Dengue Fever, Dengue Haemorrhagic Fever

INTRODUCTION

Ka-dinga pepo is the origin of "dengue." The term "ka-dinga pepo" is derived from a Swahili phrase that means "cramp-like seizure." The first epidemiological outbreak of dengue occurred in North America, Africa, and Asia in the 1780s. Earlier in 1970, only 9 countries experienced severe dengue epidemics. Perhaps, now that dengue fever occurs in more than 100 countries, the disease is considered endemic. Dengue virus is a positive-stranded RNA virus that belongs to the Flaviviridae family. DV-1, DV-2, DV-3, and DV-4 are 4 types of serotypes of the virus. Recently, scientists discovered a new serotype, which is DV-5, in the Sarawak state of Malaysia in 2007 and detected it in patients' blood. This DV can cause a mild to severe illness ranging from dengue fever (DF) to dengue hemorrhagic fever (DHF). Geographical distribution of dengue cases reported worldwide Cases of dengue and DHF are usually spread or transmitted by Aedes mosquitoes, which breed in

peridomestic environments and develop in tropical and subtropical regions. in order for warmer temperatures to enhance dengue virus replication inside the vector's body. Thus, the Aedes mosquitoes are quicker to spread their infection to new hosts. A warmer climate also affects the range of Aedes mosquitoes because it makes it easier for them to spend the winter in more places and lets them live at higher altitudes and latitudes. In this review, we will discuss the methods and materials that have been used, describe the differential diagnosis of dengue, differentiate the clinical features of dengue, discuss the impact on the second disease, and recommend proper treatment for dengue patients, including prevention and control strategies.(Bennett et al., 2020)

MATERIAL AND METHODS

There are four articles that have been examined in terms of their methods and the materials that they use. The majority of the articles focus on the planning and execution of studies, data analysis, and the definition of concepts. Nonetheless, each method followed the categorisation and clinical appearance flowchart for dengue infection.

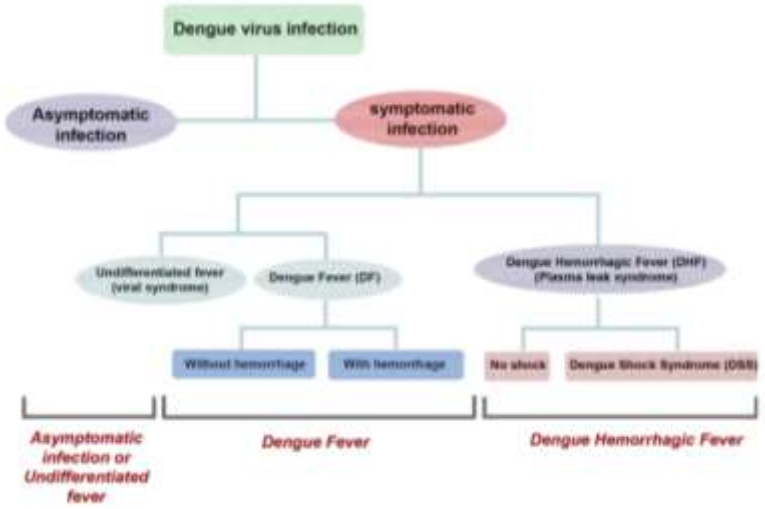

Figure 1: The classification of DENVs infection illustrated according to WHO 1997 Dengue hemorrhagic fever: Diagnosis, Treatment, Prevention and Control, 2nd edition.

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Study design and sample

Four of the articles that have been reviewed suggested that these studies involve observational and cross-sectional research. This information comes from my reading of those articles. In order to get a representative sample of all of the people who took part, they also used a technique called cluster random sampling (Wang et al., 2020). In each of these studies, the primary dengue infection was defined as detectable by IgM or NS1 and false IgG results, whereas the secondary infection was defined by IgM or NS1 and IgG results that were positive (Faridah et al., 2022). Since the primary infection is more contagious than the secondary infection, this distinction was drawn (Wang et al., 2020).

On the other hand, the vast majority of the articles collect all of the necessary information and data

from the patients in their respective covered areas through the use of survey methods. First before respondents were given the questionnaire, their contact details, the type of residence they occupied, and their prior informed consent were recorded. The questionnaire included the demographic profiles and characteristics of the respondents, as well as their knowledge, attitudes, and beliefs regarding dengue fever prevention, as well as their level of adherence with the PSN 3M Plus DHF control measures (Faridah et al., 2022).

Data analysis

In contrast to the other three articles, the first article that was observed used two distinct kinds of materials in its data analysis. These materials included Polygenic risks, core analysis and derivation with validation cohorts for various ancestries (Faridah et al., 2022). Both of these methods were employed to test for the possibility of polygenic risk for DENV infection outcome, as well as to examine the effect of a PRS applied to a validation cohort composed of individuals of all ancestries and to compare other syndromes (Faridah et al., 2022).

The remaining three articles use the collected data by coding it and entering it into worksheets. After that, SPSS was used to resolve and interpret data by using IBM SPSS 25 (Minarti, 2021). Following that, we summed up all of the primary characteristics as well as the clinical features by assigning frequencies and percentages to each group. In order to analyse the data, descriptive statistics were utilised, and the Chi-square test was utilised so that we could determine the relationships that existed between all of the variables (Minarti, 2021).

Concept definition

Other than that, this methodology has only been used in articles with title "Dynamic Changes of Platelet and Factors Related Dengue Haemorrhagic Fever: A Retrospective Study in Indonesian" and "Community Knowledge and Attitudes about the Transmission of Dengue Haemorrhagic Fever and Its Relationship to Prevention Behaviour in Palembang, South Sumatra, Indonesia." People's knowledge, treatment methods, and behaviour toward disease prevention are all influenced by their beliefs about health and how they should behave, according to both articles (Faridah et al., 2022). Specifically, the respondents' knowledge of DHF includes their understanding of the disease's clinical symptoms, the risk of contracting DHF, treatment methods, disease vector modes of virus transmission, and prevention methods. It was also stated that health beliefs comprise general perceptions of health and disease as well as sociodemographic factors (Pare et al., 2020).

Quality control and Overall effect

This control and medium effect method was used to examine the relationship between PRS and each of the three comparisons, excluding the first article mentioned previously. This is because they must identify genetic associations in three distinct correlations during the analysis of the entire recursive cohort for the first article. Where they use to fit the logistic regression model by comparing the second to fourth quartile PRS to the initial one (the referent), adjusting for age and sexual orientation in each validation ancestry, the first is made reference to as the referent (Pare et al., 2020).

RESULT AND DISCUSSION

Diagnosis

According to all articles reviewed, the effects of all three DENV infection outcome comparisons

were comparable in direction and magnitude. When the PRS for DF versus controls was applied to a validation cohort for DHF versus controls, the effect size was identical to previous estimates (Wang et al., 2020). Among the hypotheses that explain the DHF are changes in viral pathogenicity, genetic predisposition, cytokine storm, lipid profile, and immune enhancement. Certain DHF patients have never been exposed to DENV-, meanwhile the majority of DHF patients are infected with two serotypes (Wang et al., 2020). Due to thrombocytopenia, coagulopathy, instability of epithelial cells, and thrombi, patients with dengue can bleed. The impacts of the enhancement of previously existing dengue antibodies, dysregulation of cytokines, and modifications to the lipid profile were summarised (Singh et al., 2020).

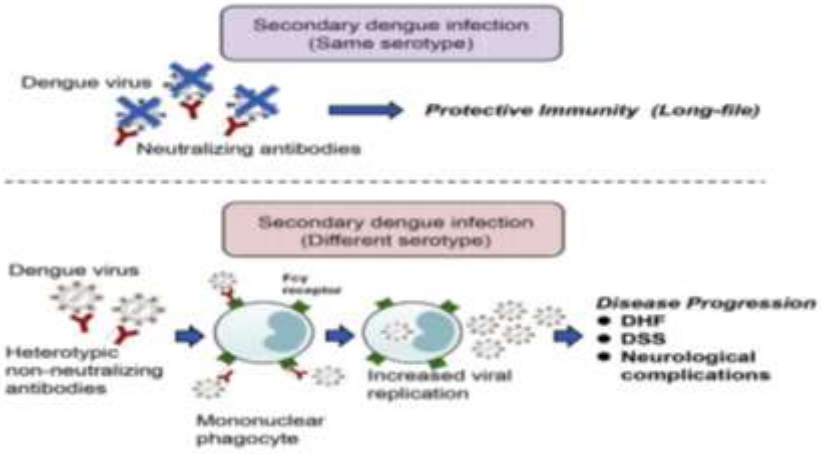

Figure 2: The methodology of antibody-dependent dengue virus infection enhancement.

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Despite this, each research has linked the intensity to Antibody-dependent amplification. Residual infections with the same serotype are obligated and neutralised by antibodies produced by the immune system, whereas secondary heterotypic infections may be more drastic. In general, secondary heterotypic DENVs infectious disease through ADE exacerbates disease severity (Singh et al., 2020). This phenomenon should be considered when creating a dengue vaccine intended to safeguard against all four serotypes by dispensing four antigens in a single shot. Among the indicators of DENV infection are cytokine profiles (Venkataramanan et al., 2019). The production of cytokines in the peripheral blood mononuclear cells of subclinical DENV patients differed considerably based on clinical manifestation. The PBMC of DENV patients with symptoms released IL-15, MCP-1, and IL-6. Mild or non-dengue syndrome patients secreted IL-12, IL-2R, MIP-1a, RANTES, GM-CSF, and TNF (Singh et al., 2020). In addition, lipoproteins contribute to the pathophysiology of the immune response to the changes in lipid profile stimulated by cytokines which may also predict the clinical outcome of DHF. There is a correlation between DHF and changes in plasma total cholesterol, HDL, and LDL.

Clinical Features

According to WHO criteria, 43.05% of patients were diagnosed with DF, while 56.95% had DHF. The highest incidence of dengue was among adolescents (12–21 years), followed by young adults (21–45 years) and children (2–12 years) (Faridah et al., 2022). The DHF group had a greater

proportion of male patients (55.9%) than the DF group (46.9%). In addition to fever, dengue patients frequently presented to the hospital with nausea/vomiting (66.97%), headache (35.79%), and abdominal pain (21.7%) (Faridah et al., 2022). DHF patients exhibited significantly higher rates of nausea/vomiting and abdominal pain compared to DF patients. The prevalence of fatigue was significantly higher in the DF group compared to the DHF group.

However, no correlation was found between gender, age, education, or occupation and PSN 3 M Plus compliance. Theoretically, elderly persons have significantly larger compliance and adherence with PSN 3 M Plus. Sukesi et al. found that individuals with a higher education level are less compliant with DHF prevention practises. Despite this, the study discovered that working respondents are less compliant with DHF prevention practises than non-working respondents and housewives. This is consistent with a previous study's finding that economically inactive informants were among the most likely to engage in DHF prevention measures.

Discussion

Impact Of Second Infection

The risk of developing a severe infection after having been exposed to the dengue virus more than once is growing. After being exposed to any one of the four serotypes of the dengue virus, a patient will have temporary immunity to all of those different strains of the virus for a period of time following their infection. Over the course of two to three months, immunity to the other serotypes diminishes, leaving the patient with lifetime protection exclusively against the serotype with which they were infected. If the patient is exposed to one of the other serotypes, he or she is at an elevated risk for a severe illness, including DHF and DSS. This appears to be the result of an antibody-dependent improvement. The virus enters cells whose membranes have Fc-receptors. This boosts viral replication and, thus, the viral burden of the patient. A higher viral load is associated with a more severe illness course. As the total number of dengue cases rises, the likelihood of more severe cases increases considerably. (Aryu Candra, 2010)

Two ideas or hypotheses continue to be debated about the immunopathogenesis of dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS): secondary infection (also known as secondary heterologous infection), and antibody dependent enhancement (ADE). According to the described theory or hypothesis of secondary infection, when a person acquires secondary infection with a single virus serotype dengue, a long-lasting immune response will develop against infection with the dengue virus serotype. However, this is not the case if the infection is acquired due to dengue virus serotypes. Otherwise, a grave infection will develop. This occurs as a result of heterologous antibodies formed during primary infection, which will form complexes with different new dengue serotypes that cannot be neutralised even when inclined to do so. The complex will then be internalised, activated, and produce IL-1, IL6, tumour necrosis factor-alpha (TNF-A), and platelet activating factor (PAF), resulting in an increase in dengue virus infection. The mechanism by which TNF-alpha causes blood vessel wall permeability, plasma fluid leakage, and vascular endothelial injury is not well understood. Another theory explains that the immune complex that is generated will stimulate the complement in a pharmacologically quick and brief manner. Additionally, the immune complex is vasoactive and procoagulant, which causes plasma to leak out, resulting in shock and hypovolemia, and bleeding. As a result of prolonged infection, non-neutralizing antibodies develop in the bodies of infants younger than 2 years old whose mothers are infected with the dengue virus and who transmit the infection to their infants. In the event that a child is infected with the dengue virus, an amplifying process will instantly take place, stimulating

readily infected and activated macrophages to secrete IL-1, IL-6, TNF alpha, and PAF. (Mangold, 2013) According to the ADE theory, if there are specific antibodies against a certain virus type, the disease produced by the virus can be prevented; but, if the antibody cannot neutralise the virus, the virus will actually cause serious sickness. IgM, IgG1, and IgG3 predominate in the kinetics of dengue virus-specific immunoglobulin in the sera of patients with dengue fever, dengue hemorrhagic fever, and dengue shock syndrome.

In addition to these two theories, there are more theories about the pathogenesis of DHF, including the theory of viral virulence based on serotype variations. Dengue viruses DV-1, DV-2, DV-3, and DV-4 have all been identified in fatal cases, however regional variations exist. Then there is the patient- or event-specific antigen-antibody theory. In DHF, there is a decline in system activity in addition to a significant reduction in levels C3, C4, and C5. In addition, between 48 and 72% of DHF patients have complex immunity between IgG and dengue virus that can adhere to platelets, B cells, and other body organ cells, influencing the function of system components and other immunity. In addition, the moderator theory suggests that macrophages infected with the dengue virus would release different mediators, such as interferon, IL-1, IL-6, IL-12, and TNF, which, along with endotoxins, cause septic shock, fever, and increased capillary permeability. In dengue virus infection, viremia occurs very rapidly, and in just a few days, infection can spread to multiple sites. However, the level of tissue loss (tissue destruction) induced is insufficient to cause death from a viral infection; most deaths were due to metabolic problems.

Treatment

There is not yet a specific antiviral medicine available, nor a vaccine that has already been authorised for use in the treatment or prevention of DENVs infection. (Swaminathan et al, 2019). This is the case at the present time. There is still a significant danger to people's health all around the world due to DF and DHF. Recent epidemics of dengue fever have been linked to DHF, which has been associated with significant fatality rates. Due to the complex nature of its aetiology, we do not yet understand the factors that contribute to the development of DHF, despite the fact that this condition poses a significant health risk. (Thai et al., 2011)

Supportive care is the foundation of treatment for dengue infection because there is apparently no antiviral medicine that can specifically target the dengue virus. Because nonsteroidal anti-inflammatory medications might impair coagulation, medical professionals should steer clear of prescribing ibuprofen for the patient's fever and pain. It is recommended that Tylenol be used as both an antipyretic and an analgesic. Patients who are expected to make a full recovery from their condition should be encouraged to drink plenty of fluids and rest in bed. During the feverish stage of a disease, this is typically something that can be done at home. Because the initial diagnosis of a mild course during the febrile phase can swiftly progress into a severe disease during the critical phase, these patients should have close follow-up. On days 3 through 7 of their child's illness, parents should be informed to look for indicators of DHF or DSS in their children as their fevers begin to decrease.

Prevention And Control Strategies

In order to prevent patients from contracting dengue fever frequently, preventative and control techniques are crucial. Physical, biological, and chemical control are the three basic elements of preventive and control mechanisms. Physical control methods include society-based control programs. Society based control strategies are build among people to educate them on ways to

eradicate mosquito breeding habitat. Several strategies can be combined for maximum control of the vector population through community involvement. The programs that approach to minimise the volume of mosquito breeding grounds include educating people, cleaning activities, removing unwanted water-collecting habitats in bottles to eliminate larvae breeding. All these activities help people to create an awareness on ways to eliminate breeding of eggs and larvae which later develop into vectors that cause infectious disease.

Following that, biological control is used to reduce pest population by using biological organisms. Wolbachia bacteria is the most common biological organism that is used to control the population of Aedes mosquitoes. Wolbachia carries mosquitoes, whereby this bacterial species is injected into the mosquitoes and gradually colonizes the mosquito's population. This bacteria able to reduce the vector population by interrupting their sexual cycle. (Niang et al., 2018). Other than that, use of sterile insect technique which is also known as STI continuously helps to suppress mosquitoes which causes major infection such as hemorrhagic dengue fever. This technique is basically, releasing laboratory sterilized male mosquitoes in the targeted population. Once it is released, these male mosquitoes help to reduce female mosquitoes' reproduction percentage, which helps reduce the number of vectors in metropolitan areas. Another biological control strategy is to use larvivorous fish and crustaceans which help to reduce vector larvae populations. The use of larval fish to manage mosquito breeding habitat, because the fish species would eat the mosquito larvae and pupae which are able to destroy the growth of vectors.

Moreover, the chemical control method is the easiest way to kill and control the vectors of dengue fever. Chemical agents such as insecticides are used to repel, and kill Aedes mosquitoes and other insects that cause life threatening diseases. Chemical larvicides have been proven to be effective against container-breeding Aedes mosquitos in clean water, including organic synthetic insecticides like temephos (Abate) and insect growth regulators (IGRS) like methoprene (Altosid, juvenile hormone mimic). If the following chemical larvicides are utilised properly in human settings, they have very little of an environmental impact. (Gan et al., 2021)

As we know there is no specific vaccine for dengue fever, however some studies and research show live, attenuated dengue vaccines offer protection against repeated dengue infections. This vaccination can provide up to 84% protection against the occurrence of a severe dengue infection, and 82% protection against experiencing symptoms of the virus in people who have already had the disease. Therefore, people must be always aware of their environment hygiene, avoid getting bitten by mosquitoes, limiting their breeding site and getting vaccines to protect them from getting infected. (Wilder-Smith, 2020)

CONCLUSION

To conclude, dengue hemorrhagic fever causes severe illness and can even cause death if untreated. A person usually has low immunity after contracting dengue fever for the first time because they tend to lose the majority of their antibodies. Due to their low antibody levels and compromised body immune systems, if they contract the infection a second time, this could result in a more serious illness. The dengue virus can harm our immune system by eliminating vast quantities of antibodies in the body, thus it is crucial to always take precautions to avoid contracting it. The virally infected person needs to start seeking therapy right away to prevent further complications and serious conditions. Treating symptoms and providing supportive care for dengue patients are both crucial.

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