Early Detection of Plasma Leakage in Dengue Hemorrhagic Fever

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Dengue viral infection remains a major public health problem. As many as 400 million people are infected yearly.[1] Even though the vaccine is available, the use of dengue vaccine is still limited due to some concerns. Among patient infected with dengue viral infection, early recognition of the virus and prompt supportive treatment are important to avoid complication and mortality.

The clinical spectrum of dengue viral infection is diverse ranging from undifferentiated fever to dengue shock syndrome characterized by plasma leak and hemoconcentration.[2] No specific antiviral therapy is available. Therefore, anticipation of complication should be performed adequately.

The most dangerous complication of dengue infection is shock syndrome. Hypothetically the occurrence of shock is a result of secondary viral infection. The manifestation of increased vascular permeability and low intravascular volume lead to the development of shock.[3] In addition to that, another complex mechanism underlies the occurrence of shock such as endothelial dysfunction that could happened abruptly. No specific method exists to identify this condition as early as possible.

During dengue infection, fever can be last between 2 and 7 days. The localized plasma leakage could happen and manifested as a pleural effusion fluid accumulation in abdominal cavity or hemoconcentration. This will only last for 48 hours and will be resolved later spontaneously.[3,4] Severity of leakage varies among patients and the unanticipated of leakage due to failure to recognize and treat this manifestation related to mortality.[2-4]

Most of the fatal cases of dengue are related to late detection of the illness as shown by massive hemorrhage and severe intravascular volume depletion. The role of dendritic cells is as the initiator of immune response that facilitate virus uptake.[4] On the other hand, the non-neutralize cross reactive antibodies will increase virus uptake and resulted in more viral replication. Some studies showed higher NS1 protein were found in patients with more severe disease. In addition to that antibody to NS1 could bind to the endothelial cells and lead to apoptosis of these cells. Both host and viral factors contribute to the severity of the illness.

One of the important factors for dengue viral infection is the capacity of clinicians to identify the risk factors for shock. Studies reported that female, infants, elderly, patients with concomitant diseases are prone to have more severe infection.[5-7] Virus serotype and genetic susceptibility may also contribute but the evidence is still limited. So, those are not sensitive enough be used in clinical setting.

Besides those, after the diagnosis of with dengue infection based on WHO criteria and confirmation by serology detection or viral material in the blood, no specific sign and symptoms are available to determine any potential severity. There were studies performed to monitor the plasma leakage using mean arterial

blood pressure (MAP) instead of hematocrit values. Rapid intervention can be administered by monitoring MAP to avoid deleterious consequences.[8,9]

The classification of WHO 1997 or 2009 were not able to detect the plasma leakage earlier.[10,11] Nainggolan et al[12] presented the resulted of their observation among early dengue infection which was the occurrence of gallbladder wall thickening as a manifestation of plasma leakage. Ultrasonographic measurement is valuable and applicable to detect plasma leakage in earlier phase with positive likelihood ratio 2.14 (95% CI 1.12 – 4.12). Similar report from Indonesia also showed the role of ultrasonography in dengue.[13]

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