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Dengue hemorrhagic fever: Comparison of patients with primary and secondary infections

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Summary
Background: Dengue hemorrhagic fever (DHF) is considered to be associated with secondary dengue infection. This study was conducted to note frequency of primary and secondary dengue infection in DHF patients. Additionally these patients were compared in terms of age, gender, laboratory parameter, diseases severity and outcome.
Materials and methods: In this cross sectional observational study DHF patients fulfilling DHF criteria of Dengue Expert Advisory Group (DEAG) were included and divided into groups based on dengue specific IgG positivity and ratio of IgM to IgG. Group I, patients with secondary dengue infection were IgG positive or their ratio of IgM to IgG was <1.2. Group II, primary dengue infection patients were IgG negative or their ratio of IgM to IgG was >1.2. The two Groups were compared for statistically significant association in terms of age, gender, laboratory parameter (at admission hematocrit [HCT], platelet, white blood cell [WBC] counts, alanine aminotransferase [ALT] value), severity (DHF or dengue shock syndrome), and outcome (recovered or expired).
Results: Two hundred thirty-four DHF patients were included. 66.2% was male and 33.8% female. Mean patient age was 28.8 ± 12.4 years. Based on dengue markers results, 61.5% patients were categorized to Group I, and 38.5% to Group II. Statistically significant association between the two Groups was noted in terms of at admission platelet count, and ALT value, P value <0.05.

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Conclusion: Primary dengue infection is frequently associated with DHF. Patients with DHF caused by secondary dengue infection have lower at admission platelet counts and higher ALT value.

Introduction

Dengue is arthropod-borne viral illness caused by infection with one of the 4 serotypes of dengue virus. Dengue viruses are RNA viruses that belong to the Flavivirus genus. Dengue is an important global health care issue. At least 3.6 billion people living in more than 125 tropical and subtropical countries are at risk of developing dengue infection [1]. Internationally, up to 22,000 deaths are attributed to dengue per year [2].

Dengue infection can result in dengue fever (DF) and dengue hemorrhagic fever (DHF). The latter is further divided into four grades depending upon severity [3,4]. Infection with one of the dengue viruses confers lifelong immunity to that serotype. If a person is infected by another serotype of dengue virus (secondary infection), problematic versions of dengue, such as dengue hemorrhagic fever, may develop due to immune enhancement [4—6]. DHF can be associated with poor outcomes depending on the facilities available for patient management [3,4].

The detections of the NS1 antigen and dengue-related IgM and IgG antibodies are commonly used in dengue diagnoses [4,7]. NS1 is virus-specific non-structural protein that can be detected for up to 9 days after dengue infection [4]. IgM antibodies become detectable in most patients at days 3—5 of fever onset. Tests for NS1 and IgM antibodies have high sensitivities (~90%) and specificities (98%) in the diagnosis of dengue at ≥5 days from fever onset. IgG dengue-specific antibodies are used to diagnose prior dengue infections [4]. Various characteristics of patients with dengue infections have been the focus of extensive research. However, there is a paucity of studies that have focused on DHF patients and have emphasized primary and secondary infections.

The first outbreak of dengue in Pakistan occurred in 1994—1995. Since that time, dengue has increasingly been recognized as an important health care issue [8—10]. A dengue epidemic occurred in Rawalpindi, Pakistan from July to December of 2013 [11,12]. In this epidemic, 1175 patients suffering from dengue infections were diagnosed at public sector hospitals. Of the 811 patients who were managed at Holy Family Hospital, Rawalpindi, 255 had DHF. This study sought to note the frequencies of primary and secondary infections in DHF patients. Additionally, age, gender, severity of DHF, hematological parameters at admission (i.e., hematocrit [HCT] and platelet and white blood cell [WBC] counts), alanine aminotransferase (ALT) level, duration of hospital stay, and outcome were compared between patients with primary and secondary dengue infections.

Materials and methods

Study and participants

This cross sectional, observational study was conducted at the Medical Unit of the Holy Family Hospital, Rawalpindi from the 1st of July 2013 to the 31st of December, 2013. All patients with dengue infection who fulfilled the DHF diagnostic criteria and were managed at this hospital were evaluated. Patients with illnesses associated with hematological abnormalities, ascites and/or pleural effusion were excluded. These exclusion criteria included chronic liver disease, autoimmune disorders, hematological disorders, renal failure, etc. Patients with unknown dengue IgG statuses were also excluded from the study. The patients were managed in a standard manner as per the Dengue Expert Advisory Group (DEAG) protocol for DHF/dengue shock syndrome (DSS) [13].

Ethical considerations

This study was approved by the Departmental Ethical Committee, and the patients were included after they or their surrogates provided informed consent.

Dengue diagnostic criteria

Dengue infection: The diagnosis of dengue infection was based on the DEAG criteria [13].

DHF: DHF is characterized by plasma leakage revealed by hemoconcentration (an increase in hematocrit ≥20% above the age-adjusted average or a decrease in hematocrit ≥20% of the baseline following fluid replacement therapy), pleural