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Study Outcome of Dengue Patients with and Without the Use of Steroids

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I. INTRODUCTION

A viral disease spread by vectors, dengue fever (DF) affects tropical nations' urban and semi-urban areas [1]. An important global public health issue is dengue fever [2]. It is brought on by the four serotypes of the dengue virus, which are flavivirus-related arboviruses [3]. The mosquito Aedes aegypti is the disease's vector [3]. Dengue fever is endemic in most of India's regions [1].

Dengue cases have been rising over the past few years. A total of 28292 cases were reported in 2010, rising to 50222 in 2012 and 75808 in 2013, the most cases reported since 1991. Following the compilation and distribution of the national clinical care guidelines of dengue in 2007, the case fatality ratio/ 100 cases decreased from 3.3% in 1996 to about 0.4% by 2010. In 2013, this further decreased to 0.3% [4,5].

Dengue's clinical course can range from a non-specific febrile sickness to a serious and occasionally fatal condition. Increased vascular permeability and impaired haemostasis are common symptoms of transient vasculopathy, which often develops 3-6 days following the start of a fever is one of the most frequent consequences seen. The majority of specialists concur that dysregulated host immunological responses, especially those linked to secondary infections, are what generate the vasculopathy that characterises severe dengue [6]. There are currently no vaccines or licenced medications for the condition, thus supportive care is the sole method of management.

Numerous diseases with immunological derangements have been demonstrated to benefit from high dosages of corticosteroids as immune system modulators. However, there is controversy around their clinical application in septic or inflammatory shock. When sepsis causes adrenal insufficiency in patients, studies done over the past 20 years have showed tremendous promise for treating septic shock [7]. Because this debate has not yet been resolved, the current guidelines for the treatment of severe sepsis only propose corticosteroids at low quantities (i.e., hydrocortisone 200 mg daily by continuous infusion) for patients with refractory shock. Additionally, they oppose a distinction between patients who have and do not have a proper adrenocortical response [8].

Despite this, corticosteroids are often safe in sepsis with the main clinically important side effects being hyperglycaemia and hypernatremia [9]. Though there have been worries in the past, these concerns are mainly baseless, corticosteroids do not enhance the risk of superinfection and gastrointestinal haemorrhage [9,10]. Low-dose corticosteroids are thought to help septic shock patients because they restore their vascular sensitivity to vasopressors, not because of their immunosuppressive effects. The results from severe sepsis cannot be immediately generalised to dengue since it is believed that lack of vascular response to vasopressors is not the primary mechanism of shock in dengue.

High-dose corticosteroids reduced the levels of TNF-alpha, IL-1, IL-6, and IL-8 in acute respiratory distress syndrome [11], although dexamethasone had no impact on cytokine levels in dengue [12]. Another recent study, that was a part of a randomised controlled trial to determine the effects of high-dose corticosteroids given early in the course of dengue infection reported no reduction in the levels of acute phase plasma cytokine concentrations with corticosteroid treatment [13].

In order to prevent dengue sequelae and lessen the severity of the infection, there are very few studies that have examined the risks and benefits of early dengue illness treated with corticosteroids. Thus, the current study compared the results of dengue patients who received steroid treatment and those who did not.

II. DISCUSSION

A viral disease spread by vectors, dengue fever (DF) affects tropical nations' urban and semi-urban areas [1]. Dengue's clinical course can range from a nonspecific febrile sickness to a serious and occasionally fatal condition. Most experts agree that the vasculopathy that defines severe dengue is due to dysregulated host immunological responses, particularly those linked to secondary infections [6].

There are currently no approved drugs or immunizations, thus the only method of treatment

is careful supportive care. Corticosteroids in high dose were shown to be effective immune system modulators in a variety of immunological-deranged illnesses. However, their clinical application in septic or inflammatory shock has been controversial. In order to prevent dengue sequelae and lessen the severity of the infection, there are very few studies that have examined the risks and benefits of corticosteroid therapy in early dengue infection. Thus, the purpose of the current study was to compare the outcomes of dengue patients treated with and without steroids.

A total of 170 patients with dengue NS1 and IgM positivity were included in the study. "Case group" refers to patients who got oral/IV Steroids. "Control group" cases were those who did not get IV oral/IV Steroids. Following that, patients were observed daily to check for the emergence of DHF or DSS, along with routine clinical checks until death or discharge and daily platelet counts. Results from cases and controls were compared.

The average age of dengue cases was 46.67 years, and one-third of them were between the ages of 21 and 40, and another one-third of them were between the ages of 41 and 60. 56.5% of dengue patients were male, compared to 43.5% of female cases.

The demographic distribution found in this study was consistent with that of other Indian Studies. In their analysis of 115 cases, Laul et al. [61] found that the average age was 31.7 years, with 64 (57%) men and 51 (44%) women. In a similar vein, Gandhi K et al. [62] found that the median age of their sample of 53 patients was 34.3 years, with 17 (63%) men and 10 (37%) women.

These results demonstrated that dengue fever is more common in men and affects the younger population more than the elderly. This can be ascribed to younger people participating in outdoor activities more frequently than older people, especially men.

In the current study, we found 68.2% cases of dengue fever and 31.8% cases of severe dengue, often known as dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). In these 31.8% cases of severe dengue, steroids were administered.

72.8% of the patients in the study by Narayanan M. et al. [63] had DF, 18.6% had DHF, and 8.4% had DSS. 67% of patients in a study identical to this one's by Bhatt et al [64].'s were of DF, 39% had DHF, and 4% had DSS. 50.4% of the cases in research identical to this one by Laul et al. [61] were of DF, while 38.8% and 11.8% of the cases were of DHS and DSS, respectively.

When compared to situations where steroids were not provided, mean platelet counts were considerably lower and mean PCV was significantly higher both at admission and discharge (p 0.01). The results of LFTs and RFTs were both worse in steroid patients. Mean hospital stay was substantially longer in the steroid group cases (p>0.05), although fever days were similar (4.51 vs 4.13 days; p-0.208). Instances receiving steroids were shown to have greater rates of complications such as infections (11.1% vs 1.7%), bleeding symptoms (40.7% vs 0.9%), and organ failure (40.7% vs 1.7%) (p0.01).

Narayanan M. et al. [63] reported similar results, with a haematocrit of 33.2 2.0% in the DF group, 35.2 5.6% in the DHF group, and 37.2 2.9% in the DSS group. Haemoconcentration was one of the main haematological abnormalities in dengue haemorrhagic fever, according to Jassirali et al [65].'s study. Haematocrit levels greater than 40% (OR = 1.88) were found by Pongpan S et al. to be significant predictors of the severity of dengue infection in their study [66]. Similar to this, thrombocytopaenia is frequently discovered in dengue fever cases. 92.6% of the cases in the Mittal Hema et al. research [67] had thrombocytopenia. The mean platelet count was 1,02,666/cu mm in the DF group, 60,909/cu mm in the DHF group, and 36,200/cu mm in the DSS group in the study by Narayanan M. et al. [63]. This demonstrates that all three groups had thrombocytopenia, although the DHF and DSS groups had lower platelet counts. This could be elucidated by the fact that DHF/DSS patient sera had greater antiplatelet IgM levels than DF patient sera [9].

The liver is the organ most frequently affected by dengue. Hepatic symptoms are caused by either dysregulated immunologic damage in response to the infection or direct viral toxicity. Serum SGPT levels were increased in 59.7% of all patients in the study by Narayanan M. et al. [63] who had the test done. 25% of DF patients, 43.6% of DHF patients, and 66% of DSS patients had high serum SGPT levels. Serum SGPT levels were raised in 57% of the participants who underwent the test in the study by Aggarwal Anju et al. [69].

Children with dengue shock syndrome were given a tapering dosage of hydrocortisone for three days in a small randomised controlled study; older children saw a statistically significant mortality benefit (8 years and over). The first proof of corticosteroids' possible effectiveness in treating dengue was provided by this study [45]. However, multiple other controlled studies using corticosteroids in DSS failed to show any advantage [47–50], and a Review of Cochrane

library found no benefit in corticosteroid treatment for dengue [51].

We found no benefits from corticosteroid medication in the current trial in terms of haematological parameters, days of fever, days spent in the hospital, or incidence rate of additional problems. We used postural drop as a measure of dengue cases' severity. When steroids were administered, the incidence of postural drop increased from 9.5% to 25.9%. Mean hospital days and temperature were equal in subjects receiving steroid medication or not, even in the subgroup of cases with postural decline.

Numerous clinicians have attempted to look at the potential use of corticosteroids in both mild and early instances of dengue fever during the past ten years. In an RCT, oral steroids at low doses (0.5 mg/kg) or high doses (2 mg/kg) were used to treat dengue by Tam DTH et al. [53]. In this investigation, the authors reported no decrease in the occurrence of shock or other known dengue virus infection sequelae. After conducting a placebo-controlled trial, Kularatne SAM et al. [54] found that dexamethasone was ineffective at raising platelet counts in dengue infection patients when given in low doses. The Shashidhara KC et al. [59] investigation likewise came to the conclusion that a high dosage dexamethasone regimen did not work to increase platelet count in patients with acute dengue fever. In a systemic analysis, Zhang F et al. [58] examined the effectiveness of treating dengue in children and adults on the prevention of shock-related fatalities and illness progression, both with and without corticosteroids or a placebo. The authors noted that there was no proof that oral or intravenous corticosteroids had any impact on death, the emergence of severe dengue sequelae such shock, severe bleeding, severe thrombocytopaenia, ascites, or ICU admissions.

A number of the investigations also produced contradictory findings. According to the results of the Bhalla A et al. [60] study, a single dose of methylprednisolone avoided the progression of dengue fever with warning signs to DHF/DSS, permitted a higher rise in platelet counts, sped up the resolution of alarm signals, shortened hospital stays, and reduced the need for platelet transfusions. In a systemic assessment, Senaka Rajapakse et al. [55] came to the conclusion that in non-randomized trails, corticosteroids given as rescue therapy for severe shock may be beneficial. In certain studies that employed steroids in high or repeated doses, favourable therapeutic benefits were shown, according to S.M. Rathnasiri Bandara et Al systemic.'s review [56]. Using a steroid with a higher affinity for receptors and sustaining therapeutic blood levels of corticosteroids for a long enough period of time are required for corticosteroids to be successful in treating dengue.

To sum up, findings from the current investigation and several randomised control trials and systemic reviews revealed that corticosteroids given to patients with severe dengue do not improve haematological parameters. Additionally, there was no change in the length of hospitalisation and the number of days with a fever. Additionally, the steroid regimen failed to reduce the problems linked to severe dengue. Nevertheless, a few other researchers found the opposite. However, based on our findings, the current study does not advise using steroids, even in cases of severe dengue.

III. SUMMARY

The Department of Medicine at Kasturba Medical College (Manipal Academy of Higher Education), Mangalore, undertook a hospital-based observational study. Comparing the results of dengue patients who received steroids with those who did not was the study's objective. 170 patients with dengue NS1 and IgM positivity were included in the study. "Case group" refers to patients who got oral/IV Steroids. "Control group" cases were those who did not get oral/IV Steroids. Following that, patients were observed daily to check for the emergence of DHF or DSS, along with routine clinical checks until death or discharge and daily platelet counts. Results from cases and controls were compared. Following observations were made during the study:

1. Mean age of the cases with dengue was 46.67 years.
2. Male predominance was seen among cases of dengue with 56.5% males to 43.5% females.
3. Steroids were given in 31.8% cases of severe dengue.
4. In the majority of the cases, steroid was given for a week or less (94.4%) while in 5.6% cases, steroid was given for more than 7 days.
5. Mean age was comparable in cases where steroid was given as compared to cases where steroid was not given (p-0.43).
6. Male predominance was seen in both groups i.e., cases with and without steroid use (p-0.32).
7. Mean H-score was significantly more in cases where steroid was given ($p<0.01$).
8. Mean platelet counts were significantly less while mean PCV was significantly more, both at admission and discharge in cases where steroid was given ($p<0.01$).

9. Mean creatinine levels were significantly more in cases where steroid was given (1.51 vs 0.95 mg%; p<0.01).
10. Mean liver function tests parameters were significantly higher in cases where steroid was given (p<0.01).
11. Incidence of postural drop was 25.9% in cases where steroid was given as compared to 9.5% in cases without steroids (p<0.01).
12. The steroid group's mean hospital stay was significantly more (6.08 vs 4.49 days; p<0.01).
13. The steroid group's mean hospital stay was significantly more, both in cases with and without postural drop.
14. Complications like infections (11.1% vs 1.7%), bleeding manifestations (40.7% vs 0.9%) and organ failure (40.7% vs 1.7%) were observed to be higher in cases receiving steroids (p<0.01).

IV. CONCLUSION

Steroids were administered in one-third of the dengue cases in the current investigation. Steroids administered in cases of severe dengue do not enhance haematological markers. Additionally, there was no change in the number of days with a fever and the length of hospitalisation, both of which were shown to be much longer in cases where steroids were administered. Even in the patients who had postural drop, the steroid therapy did not considerably shorten the hospital stay. Additionally, steroid regimen failed to reduce the problems linked to severe dengue. Therefore, the current study does not advise using steroids in situations of severe dengue.