Dengue in End Stage Renal Disease Patients – A Case Series from a Tertiary Renal Centre of Bangladesh

MASRURA JABIN[a], MAMUN MOSTAFI[b], AHMED SHAHRIAR[c], SAAD BIN ALAMGIR[c], TANVIR CHOWDHURY[c], MST. ARIFA BILLAH[d], NAHIDA NUSRAT[d], SHATABDI ROY[d], SHUHANUR RAHMAN[d], GOLAM SARWER[d], SUSHMITA DAS[d]

Introduction:

Dengue is a mosquito-borne disease, transmitted by the four antigenically distant serotypes (DENV 1-4) affecting millions of people globally. The increase in dengue cases is attributed to global travel and climate change. As per a World Health Organization (WHO) report, dengue fever is presently endemic in 128 countries, with approximately 3.6 billion individuals residing in regions susceptible to disease transmission. This results in an estimated 390 million cases occurring annually, with around 96 million cases displaying varying degrees of clinical symptoms[1].

The Ministry of Health and Family Welfare of Bangladesh reported a total of 226224 laboratory-confirmed dengue cases and 1096 related deaths From 1 January to 9 October 2023, with a case fatality rate (CFR) of 0.5%[2].

The clinical manifestations of dengue range from asymptomatic to life-threatening cases. In 2009, the WHO established warning signs to predict severe dengue, recommending admission for patients with warning signs(eg. abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, hepatomegaly-liver enlargement by >2 cm and

an increase in hematocrit, concurrent with a rapid decrease in platelets[3,4]. Pre-existing comorbidities are also predictive factors for severe dengue. Conditions like diabetes mellitus, hypertension, chronic kidney disease, cardiac disorders, and advanced age have been associated with an increased risk of dengue shock syndrome or severe dengue[5, 6,7,8].

Here, we report 5 cases of End stage renal disease hemodialysis patients who were infected with Dengue virus.

CASE 1: A 58-year-old woman, a known case of End stage renal disease (ESRD) with Hypertension undergoing maintenance hemodialysis (MHD), was admitted with a history of intermittent fever over the last 5 days, accompanied by loose stools, nausea, and abdominal pain. Her Dengue NS1 test yielded a positive result.

Upon admission, her platelet count was 91,000/cmm, white blood cell count was 7,500/cmm, hemoglobin level was 11.6 gm/dl, and serum creatinine was 9.95mg/dl. Her platelet count increased to 148,000 /cmm on the 3rd day of admission but then gradually declined, reaching its lowest point at 82,000/cmm on the 6th day of admission. Notably, the patient did not experience any bleeding manifestations. Her SGPT was 203 U/L, and SGOT was 416 U/L on the 2nd day of admission but normalized before discharge. Additionally, mild bilateral pleural effusion was observed, which subsequently resolved.

The patient's management primarily included appropriate hydration. Within a day after admission, the patient became afebrile, and the loose motions subsided. Blood pressure was well-maintained, and she received regular scheduled hemodialysis along with other supportive treatments. Hemodialysis was heparin free till the platelet count was normal. After six days of hospitalization, the patient was discharged and continued with regular hemodialysis, following routine follow-up care.

a. Masrura Jabin, Associate Professor, Department of Nephrology, Gonoshasthaya samaj vittik medical college and Hospital.

b. Mamun mostafi, Head of Department of Nephrology, Gonoshasthaya samaj vittik medical college and Hospital

c. Ahmed Shahriar, Saad bin Alamgir, Tanvir Chowdhury, Registrar, Department of Nephrology, Gonoshasthaya samaj vittik medical college and Hospital.

d. Mst. Arifa Billah, Nahida Nusrat, Shatabdi Roy, Shuhanur Rahman, Golam Sarwer, Sushmita Das,Medical officer, Department of Nephrology, Gonoshasthaya samaj vittik medical college and Hospital.

Address of Correspondence: Masrura Jabin, Associate Professor, Department of Nephrology, Gonoshasthaya samaj vittik medical college and Hospital.

CASE 2: A 35 years old female, known patient of ESRD due to Glomerulonephritis with Hypertension, was admitted with fever of 5 days with shortness of breath, nausea and anorexia. Her Dengue IgM antibody was positive. She had right sided pleural effusion and a mild ascites with hyponatremia (Na: 129 mmol/L) upon admission. Her serum creatinine was 11.78 mg/dl. Her lowest platelet count was 82,000/cmm on 6th day of admission and her hemoglobin dropped to its lowest point of 5.1 on 3rd day because of melaena. After getting 3 units of Packed Red Blood Cell (PRBC) her Hemoglobin became 10.1gm/dl on 6th day. She received anti ulcer therapy with six doses of intravenous tranexamic acid. She also received heparin free modified slow low efficiency dialysis (SLED) till her clinical status became stable.

The patient could not be evaluated in details as left the hospital against medical advice because of financial reason. The next week patient reported to OPD clinic. At present, the patient remains stable and undergoes hemodialysis twice a week.

CASE 3: A 30 years old female, known patient of ESRD on MHD with hypertension, with Hepatitis c virus positive (not on anti-viral treatment) was admitted with fever of 6 days, loose motion, anorexia, abdominal pain for last 2 days. Her NS1 was positive, she had electrolytes Imbalance (Na- 128mmol/L, K- 6.9 mmol/L) at the time of admission. Her platelet count was 165,000 /cmm, Hb: 12.9 gm/dl, Total WBC: 10,280/cmm and Hematocrit 38.9%. Her platelet count was lowest on 5th day of admission (51,000/cmm).

The patient received comprehensive supportive care and adequate hydration throughout her hospitalization. She adhered to her regular hemodialysis schedule and remained hemodynamically stable. Following eight days of hospitalization, she was discharged with appropriate guidance and a plan for routine follow-up.

Case 4: A 55 years old male, known patient of ESRD due to Diabetic mellitus and Hypertension on MHD with Ischemic heart disease was admitted to ICU with fever of 3 days and shortness of breath for 1 day.

Table-1

Clinical and laboratory parameters of cases presented

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
Age in years	58	35	30	55	48
Co-morbidities	HTN	Glomerulonephritis, HTN	HTN	DM, HTN, IHD	DM, HTN
Symptoms on presentation	Fever, loose stool, abdominal pain	Fever, Shortness of breath	Fever, loose stool, abdominal pain	Fever, Shortness of breath	Shortness of breath, with features of shock
Pleural effusion	Yes	Yes	No	No	Yes
Lowest WBC count (per cmm)	7500	3600	6300	4920	7860
Lowest platelet count (per cmm)	82,000	82,000	51,000	20,000	90,000
Hematocrit %	36.6	30.5	38.9	39.5	32.7
Hyponatremia (mmol/l)	No	Yes (129)	Yes (128)	No	No
SGPT U/L	203	38	92	174	36
SGOT U/L	416	40	60	321	40
S. Creatinine (mg/dl)	9.95	11.78	8.59	6.44	5.67
S. Albumin (g/L)	32	30	27	13.8	36
Outcome	Discharged	Discharged	Discharged	Death	Discharged

The patient had features of shock, with non-recordable blood pressure and a SPO2 level below 78% upon admission. His oxygen saturation was maintained using a 15-liter of O2 through facemask. He was on two ionotropic agents along with other supportive care.

His dengue IgM antibody test was positive. Since admission, the patient was afebrile, with a total leucocyte count of 4920/cmm, a platelet count of 30,000/cmm, hemoglobin 8.5, hematocrit level of 35.5%, SGPT at 174 U/L, SGOT at 321 U/L, and a serum albumin level of 13.8 g/L. The patient underwent heparin free SLED hemodialysis along with albumin infusions, PRBC immediately after admission.

On the evening of the 2nd day, his SPO2 level deteriorated, leading to his placement on a ventilator. His platelet count dropped to 20,000/cmm in the evening, despite no apparent external bleeding sites. Unfortunately, the patient experienced a sudden cardiac arrest in the evening of the 2nd day and expired.

Case 5: A 48-year-old woman, a known patient with ESRD due to Diabetes Mellitus and hypertension on MHD, got admitted with a four-day history of fever and respiratory distress for one day.

During her hospitalization, she maintained her SPO2 levels with the assistance of 5 liters of oxygen through a facemask, with a recorded temperature of 102°F. The dengue NS1 test yielded negative results, but the IgM was positive. Bilateral mild pleural effusion and a urinary tract infection were also identified. Upon admission, her white blood cell count was 10,250/cmm and hemoglobin level was 11.2gm/dl, her platelet was 165,000/cmm and platelet progressively increased, peaking at 301,000/cmm on the 7th day of her stay.

The patient became afebrile on the 4th day of admission and maintained hemodynamic stability, with subsiding pleural effusion. Her antiplatelet drugs were suspended for seven days, adequate hydration was carefully maintained. She adhered to her regular hemodialysis schedule while in the hospital. After a 7-day hospitalization without further complications, the patient was discharged with follow up from OPD.

Discussion:
When considering the diagnosis of Dengue Fever (DF), it's essential to acknowledge that the symptoms can be nonspecific. Timely recognition of warning signs associated with Dengue Hemorrhagic Fever (DHF), such as intense and continuous abdominal pain, persistent vomiting, and restlessness or lethargy, is crucial for reducing mortality rates. However, diagnosing DF in patients with ESRD presents more significant challenges. The symptoms often overlap with those of uremia, making accurate diagnosis complex. Furthermore, critical indicators like hemoconcentration, pleural effusions, and hypoalbuminemia, which are part of the diagnostic criteria for DHF, may be easily overlooked in the context of uremia [9].

The presented case series describes five distinct scenarios of patients with End-Stage Renal Disease (ESRD) and varying comorbidities who were admitted with Dengue fever. Each case exhibits different clinical features, challenges, and outcomes, which contribute to a more comprehensive understanding of how Dengue affects this vulnerable population.

One striking observation is the wide range of clinical presentations, which can vary from intermittent fever with gastrointestinal symptoms (Case 1) to more severe manifestations such as respiratory distress and shock (Case 4). These variations highlight the complexity of diagnosing Dengue in ESRD patients, who may already exhibit non-specific symptoms related to their renal condition.

Thrombocytopenia, a hallmark of Dengue, was consistently observed across all cases. This thrombocytopenia was dynamic, with platelet counts fluctuating during hospitalization. Other laboratory findings such as liver enzyme elevations were inconsistent, emphasizing that organ involvement in Dengue can vary widely even within the same population.

Adequate hydration was a common thread in managing these cases, as maintaining fluid balance is crucial for both ESRD and Dengue patients. All patients continued with regular hemodialysis, which is essential for ESRD patients, even during acute illnesses. In ESRD there is a possibility of platelet dysfunction. Associated thrombocytopenia complexes the crisis much more. All patients need heparin free hemodialysis or dose adjustment of heparin during hemodialysis.

Various factors, including inflammation, affect serum protein levels. Serum proteins, vital for the immune system and tissue maintenance, including albumin. In severe Dengue cases, increased vascular permeability causes plasma leakage, leading to a drop in albumin levels. This decline in albumin may occur before other critical symptoms, making it an early warning sign of severe Dengue. According to many studies, low albumin

levels (<3 g/dl) were associated with a higher incidence of severe Dengue. Low albumin can indicate early vascular permeability changes, serving as a valuable prognostic marker, a known indicator of morbidity and mortality[11]. Hypoalbuminemia is common in ESRD that further complicates DF. Therefore, monitoring albumin levels can be a valuable tool for assessing disease severity and initiating timely interventions to manage severe Dengue cases effectively.

The financial constraints in low income group is a constant difficulty for appropriate management which was apparent in Case 2, where the patient left the hospital as she could not afford further in hospital management. It highlights the need for individualized care plans that consider financial limitations.

Maintaining electrolyte balance and effectively controlling bleeding are critical aspects of managing Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). In these conditions, capillary leakage results in a more significant issue related to fluid loss than blood loss. Consequently, the treatment strategy should prioritize the restoration of volume status and the preservation of blood pressure. In cases of DSS, insufficient fluid replacement can lead to prolonged shock, resulting in refractory shock and increased mortality . However, it's essential to strike a delicate balance, as excessive fluid administration can lead to the development of acute pulmonary edema.

The outcomes were diverse, ranging from complete recovery and continuation of regular hemodialysis (Cases 1, 3, and 5) to a high-risk discharge (Case 2) and a tragic fatality (Case 4). These varying outcomes underscore the unpredictable nature of Dengue infection in ESRD patients and the importance of prompt and appropriate care.

Case 4 is particularly noteworthy as it required intensive care support due to shock and respiratory distress. The use of inotropes and mechanical ventilation demonstrates the need for close monitoring and critical care interventions in severe Dengue cases, especially in ESRD patients.

Conclusion:

This case series highlights the challenges in diagnosing and managing Dengue in ESRD patients undergoing MHD. The dynamic clinical presentations, laboratory findings, and diverse outcomes demands the need for personalized care plans for each patient. These insights can contribute to better preparedness and care delivery for this susceptible population in regions endemic for Dengue like Bangladesh. Further research is warranted to develop more targeted and effective strategies for managing Dengue in ESRD patients.

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