



Original Article

Complications of Dengue Infection in Admitted Patients at Rehman Medical Institute: A Retrospective Study

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ABSTRACT

Dengue infection is an arthropod-borne Flavivirus infection that spread through female mosquitoes (Genus *Aedes*). Dengue infection is a major health challenge in the tropical and subtropical parts of the world. **Methods:** This is a retrospective study conducted at Rehman Medical Institute (RMI). Data were retrieved from the Clinical test reports of confirmed dengue infection during the timeline; June to October (monsoon season) of the year 2021. Clinical as well as biochemical parameters were considered during the data assembling and assessment process. **Results:** Out of 156 suspected cases of dengue infection, 94 were confirmed through laboratory testing. 83 patients tested positive with Dengue NS1 antigen while after re-screening 94 cases (54 male patients and 40 female patients) were confirmed by Dengue serology (IgM antibodies) test. According to our study results, among a set of varied symptoms, malaise (99%) was the most common clinical presentation, along with 94% fever. Some patients with severe dengue infection developed serious illnesses including encephalopathy (8.5%), hypokalemic paralysis (6.3%). Moreover, 8.5% of patients were presented with Cholecystitis seen as Edematous Gallbladder wall on ultrasound scans, and 1% of the patient developed acute Pancreatitis. Fortunately, no casualty was reported due to dengue at RMI-General hospital. **Conclusion:** In our setup, Fortunately, no death was reported but a substantial number of patients suffered from serious complications such as neurological and hemorrhagic conditions along with communal clinical manifestations. Despite much reported data still, further investigation and monitoring are needed to comprehend the contemporary condition of the prevalence of dengue infection in Khyber Pakhtunkhwa, Pakistan.

INTRODUCTION

Dengue fever has become endemic in more than a hundred countries in the last decade. The World Health Organization (WHO) estimates that 50-100 million individuals contract the dengue virus annually [1]. Dengue is endemic in Pakistan. From 1 January to 25 November 2021, a total of 48,906 cases including 183 deaths (case fatality ratio (CFR): 0.4%) were reported Khyber Pakhtunkhwa (KPK), a province bordering with Afghanistan, reported the second-largest number of cases with 10,223 cases, accounting for 21% of the total [2]. The infected *Aedes* mosquito (*Aedes aegypti*) is a major vector for the viral transmission of dengue in humans [3]. The rising morbidity and mortality rates due to dengue infection have become a fundamental problem over the recent decade [3][4]. It is a multisystemic

infection, transmitted through *Aedes aegypti* or *Aedes albopictus* mosquito bites to humans [5]. This virus is a single-stranded RNA antigenic complex belonging to the genus flavivirus family Flaviviridae. Dengue virus (DENV) has four serotypes DEN-1, 2, 3, and 4. These types are originated from sylvatic strains. Each serotype has the potential to infect a person once in a lifetime [6]. Disease severity increases many folds by subsequent DENV serotype infection. Every serotype is different in its genetic makeup and due to rapid mutations, it is difficult to obtain a vaccine that specifically targets the virus [7]. The signs and symptoms of dengue fever can range in intensity from mild to severe, it can present as uncomplicated dengue fever, dengue hemorrhagic fever (DHF), or in some cases

progress to dengue shock syndrome [8]. Commonly it is clinically manifested as a fever associated with viremia, headache, retro-orbital pain, arthralgias, myalgias, malaise, sore throat, rash, lymphadenopathy, dysgeusia, and hypogeusia. In worse cases, hemorrhage (petechiae, bleeding gums, epistaxis, menorrhagia, hematuria), plasma leakage due to increased vascular permeability [9], and thrombocytopenia (low platelets count) can also occur [10]. In the case of dengue shock syndrome (DSS), hemodynamic deterioration is life-threatening due to plasma leakage into interstitial spaces and thrombocytopenia leads to the ultimate loss of intravascular volume is responsible for this outcome. DSS is the major reason for morbidity and mortality of dengue patients [11]. Complicated and diverse manifestations of dengue infection make its diagnosis and prognosis difficult and lead to misdiagnosis and morbid outcomes [12]. Early detection of dengue complications is needed for complete recovery. Despite many studies, there is still an understanding gap about the epidemiology, clinical manifestations and complications of dengue infection of different ethnicities. Therefore, the present retrospective study was aimed to study epidemiology, diagnosis, manifestations, and treatment outcomes of dengue infection in the Pashtun ethnicity of Pakistan.

METHODS

This study was conducted at Rehman Medical Institute (RMI) General Hospital, the largest and well-equipped tertiary healthcare private hospital in the province, facilitated with 500+ beds. Situated at the gateway of the famous Khyber Pass in Peshawar, Khyber Pakhtunkhwa (KPK). A retrospective study design was used. The data was retrieved from clinical reports stored in health clot files. Only confirmed dengue cases were included. The data collection duration was 5 months (June to October-2021). Serology and molecular testing were done at the clinical laboratory testing unit of RMI Hospital according to internationally recognized procedures. The first positive dengue case came across at RMI during the second week of June and numbers continued to increase till the last week of October. No case was reported afterward. According to laboratory testing data, a total of 156 patients were investigated for dengue infection, out of which 94 patients tested positive for dengue virus. Complete information like co-morbidity and epidemiological data were also noted. The details of the clinical examinations and Serological testing results were retrieved from the health clot program file of the hospital. Test reports consisted of the results of complete blood count, hematocrit, ALT, AST, blood group, dengue specific NS1 antigen, Dengue IgM antibody, hemagglutination inhibition. Enzyme-Linked

Immunosorbent Assay (ELISA) and commercially designed Dengue Virus IgM kits and NS1 Kit were used (Nova Lisa Dengue IgM ELISA kit, DENV Detect™ NS1 ELISA Kit; In Bios International, Inc., USA) for the detection of dengue infection. Collected data was stored into Microsoft Excel sheets. Percentage of Socio-demographic data, serological data, percentage prevalence of comorbidities, clinical symptoms, and complications were calculated by using Microsoft Excel Spreadsheet Software.

RESULTS

Out of 165 suspected dengue cases, 54% (89) patients were tested positive after NS1 and upon reconfirmation by IgM serological testing 5 more patients were reported dengue positive. In total 94 (57%) confirmed dengue cases were recorded, 52% of patients had high-intensity fever, and 48% had a mild fever. According to noted comorbidities data 4% of patients had cardiovascular problems, 1% had ophthalmic disease, 22% patients had diabetes, and 6% patients had cancer. Serological and Comorbidities data are summarized in Table 1.

Diagnostic tests (Total n=165)		Outcomes (positive cases n=94)	
Dengue NS1		89	54%
Dengue IgM		94	57%
Fever Intensity			
Sever	46		52%
Non-sever		43	48%
Comorbidities (Yes) n=			
Cardiovascular Disease		4	4%
Ophthalmic Disease		1	1%
Diabetes		21	22%
Cancer		6	6%

Table 1: Comorbidities, Diagnostic tests, and outcomes of dengue cases

The results of Socio-demographic data of dengue patients are presented in Table 2. 54% of male patients were infected with dengue and 43% were females. Among these patients, 18% had a traveling history to a dengue-endemic area, mostly from Iran and Afghanistan.

VARIABLES		PREVALENCE	PERCENTAGE
Gender	Male	54	57%
	Female	40	43%
Age	1-18	0	0%
	18-33	36	38%
	34-48	45	48%
	≥49	13	14%
Occupation	Unemployed	20	21%
	Student	3	3%
	Employee	60	64%
	Businessperson	0	0%
	Daily wager	11	12%
Education status	Literate	74	79%
	Illiterate	20	21%
Residence	Ruler	27	29%
	Urban	67	71%
Travel history to any endemic area		17	18%

Table 2: Results of Socio-Demographic data of dengue patients.

Clinical manifestations and symptoms of dengue cases are

summed up in Table 3. Main complaints besides body Aches/malaise (99%) were: myalgia (94%), fever (94%) of which 52% patients had high-intensity fever and 48% had low-intensity fever, Vomiting (22%), Abdominal pain (95%), Thrombocytopenia (71%), Rash (53%), Diarrhea (39%), Cough (39%), Nausea/ Vomiting (22%) and Headache (17%) recorded.

Clinical Manifestations	(Positive), n=	Percentage (%)
Body Aches/ Malaise	93	99%
Fever	64	68%
Headache	16	17%
Nausea/ Vomiting	21	22%
Constipation	9	10%
Diarrhea	37	39%
Facial Flushing	0	0%
Conjunctival Suffusion	0	0%
Severe Backache	6	6%
Lymphadenopathy	0	0%
Arthralgia/Myalgia	89	94%
Cough	37	39%
Thrombocytopenia	67	71%
Rash	50	53%
Pleural Effusion	0	0%

Table 3: Clinical Manifestations/clinical symptoms of dengue cases

Mild dengue encephalopathy was observed in 8.5% patients; Table 4. All patients presented with headaches, seizures, and a reduced level of consciousness, sensitivity, and cognitive impairment, with personality and behavior changes, including anxiety, depression, and emotional lability. Hypokalemic paralysis was diagnosed in 6.3% of patients, presented with high-intensity fever, flaccid paralysis, and hyporeflexia without any history of similar illness. Their serum potassium was between 1.9 -2.6 mEq/dl. Potassium supplementations relieved hypokalemia complications in all patients. Related investigations for other causes of hypokalemia were negative in all cases. Results are presented in Table 4. Hemorrhagic complications were noticed in 11.7% of patients, Table 4; including Gingival bleeding (5%), Melena (1%), Skin hemorrhages (3%), Epistaxis (2%). While other acute complications were also reported, Table 4; one patient (1%) had pancreatitis (inflammation of the pancreas), 8.5% of study patients were diagnosed with Cholecystitis (edematous gallbladder) upon ultrasound scans.

Complications	Number	Percentage %
Neurological		
Encephalopathy (CNS),	8	8.5%
Hypokalemic paralysis (PNS)	6	6.3%
Hemorrhagic		
Gingival bleeding	5	5%
Melena	1	1%
Skin hemorrhages	3	3%
Epistaxis	2	2%
Other Complications		
Cholecystitis (Edematous gallbladd	8	8.5%
Pancreatitis	1	1%

Table 4: List of Complications manifested in dengue patients
Patients with the risk of developing a hemorrhagic

complication received platelet transfusions. Those with active bleeding received tranexemic acid, vitamin K, and plasma transfusions leading to positive outcomes. In the patients where electrolyte imbalances were significant the focus of treatment remained its correction. Potassium supplementation in the standard regimen was given to patients with hypokalemic paralysis which resulted in complete recovery from the paralysis. Dengue patients with gastrointestinal (pancreatitis) and hepatobiliary(cholecystitis) complications were managed conservatively with close monitoring and their status improved.

DISCUSSION

Data of the current study contributes to understanding the severity and range of complications noted in the second most dengue-stricken population (Pashtun ethnicity) of Pakistan, despite many efforts to control its spread in the region, the dengue cases are expanding every year. In this study of all age groups, dengue patients were included. Many studies of different regions reported similar complications during dengue infection. In one study, 14.6% of cases of neurological complications (central and peripheral) due to dengue fever has been reported [13]. Garg, et al. reported 4% of dengue patients with neuromuscular complications[14], In our study myalgia and hypokalemic paralysis can manifest neuromuscular complications. Kulkarni, et, al. reported 2.64% neurological complications in his study, with Encephalopathy as the commonest manifestation among dengue patients [15]. Mohanty et, al. reported 13.9% of patients with pancreatitis, 15% Hemorrhagic complications due to dengue-[16]. Tavares, et, al reported edema of the gallbladder during dengue infection [17], all these reported studies manifests the complications caused by dengue virus. In the current study, due to inherent limitations, such as retrospective nature, compact sample size, institutionalized study setup, and data sharing restrictions from patients were some of the procedural pitfalls that might affect the scientific rationality and consistency of the concluding outcome. Despite these restrictions, study findings were interpreted vigilantly and the verdicts of this study are certainly important as they elucidate time-place distributions of dengue cases with their set of complications and clinical features. Still, we need large-scale studies to understand the degree of severity and the many confounding attributes of the dengue virus infection. Dengue infection is causing high damage in low developed areas because of unawareness [18]. Furthermore, we need to take effective initiatives to control vector birth [19] and transmission at human-vector contact places (residences, workplaces,

schools, and hospitals)[20]. As it is a fact that despite many efforts no specific drug or vaccine is approved for its treatment [21], thus the implementation of various practices such as timely and appropriate diagnosis can intercept the dengue fever progress into life-threatening outcomes and can reduce its rapidly expanding impact.

CONCLUSION

In our observational retrospective study Malaise, Myalgia, Fever, and Rash were communal signs. A significant number of cases suffered from Neurological Complications, Hemorrhagic complications, and Cholecystitis (redness and swelling of the gallbladder).

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