ORIGINAL ARTICLE

A Profile of Clinical Presentation, Management and outcome of Dengue Fever in Children admitted at a Tertiary Care Hospital of Rawalpindi During 2019 Outbreak.

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Abstract

Introduction
Dengue is an important viral infection in humans. Causing a significant morbidity and mortality. About 390 million infections and 50,000 deaths occur every year world over. About 2.5 billion people in the world live in areas where Dengue transmissions occur.The Dengue patients in Rawalpindi during 2019 out break were more than 12000.The pediatric population in this epidemic is assessed in our study.

Objectives
To assess the clinical, laboratory, radiological profile, management and outcome in children upto 12 years of age presenting with dengue infection to Pediatric department of Benazir Bhutto Hospital during 2019 outbreak.

Methodology
This prospective descriptive study was conducted at Department of Pediatrics, Benazir Bhutto hospital Rawalpindi, for a duration of 6 months from July to December 2019. Every admitted case with confirm Dengue fever according to inclusion criteria was included in this study. Data was recorded on predesigned study questionare, entered and analyzed in SPSS version 24 for descriptive statistics and analysis.

Results
438 children were enrolled with the clinical diagnosis of dengue fever. Of these 254 (58%) were boys and 184 (42%) were girls. Mean age of children was 8.13 years (SD ± 3.4).Fever at presentation was seen in 95.7%, pain and body aches in 79.4%, vomiting in 54.5% and loss of appetite in 63.4% of cases. Pulse pressure of <30mmHg was seen in 38.5% cases. Thrombocytopenia, leukopenia, HCT > 20% with platelets <50,000, deranged LFTs, hyponatremia, hepato-spleenomegaly and gall bladder wall thickness on ultrasonography were Seen significantly associated with progression of disease and development of complications. 254 children were reported as uncomplicated dengue fever. 119 children developed dengue hemorrhagic fever and were manage accordingly. 65 children went into dengue shock syndrome and treated for the complications. One male child died due to multi organ failure. Average duration of hospital stay remained 2.5 days (±1.2) for uncomplicated dengue fever, 4.9 (±1.9) days for dengue hemorrhagic fever while 7.3(±2.8) days for dengue shock syndrome.

Conclusions
Most commonly affected age group was 8-12 years old with a predominance of male. Signs of plasma leak proved to be reliable indicators of the disease severity and helped in timely institution of fluid therapy according to WHO guidelines. Laboratory parameters like leukopenia, increased haematocrit ,thrombocytopenia and increased AST level were significantly associated with development of complications. All levels of health personnel must be aware of clinical signs and symptoms of all dengue types. Careful monitoring of unusual presentations early recognition of severe manifestation and timely intervention can reduce disease specific mortality rate.

Keywords
Clinical presentation,Dengue Fever, Dengue hemorrhagic fever, Dengue shock syndrome

Introduction

Dengue is an important viral illness in humans. Dengue infections have increased in recent decades.according to WHO estimates,about 2.5 billion people live in areas where dengue transmissions occur.each year about 390 million people get infected and there are more than 50,000 deaths due to dengue infection world over each year.[1] dengue fever, dengue hemorrhagic fever and Dengue shock syndrome remain leading cause of morbidity and mortality among children in some Asian countries. Most of the severe cases and deaths occur in children younger than 15 years of age.[2]

Female mosquitoes of the species *Aedes aegypti* and, *Aedes albopictus* transmit dengue virus. Aedes aegypti is primarily a daytime feeding mosquito. The transmission occurs mainly in rainy season as this produces envoirnmental conditions suitable for mosquito breeding.[3]

Clinical features develop in about 3 to 14 days after mosquito bite and may persist for up to a week. Chikungunya, yellow

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fever and zika virusesare also transmitted by these viruse.[3] Dengue virus (DENV) belongs to Flaviviridaefamilyand is an RNA virus.[4] There are 4 Dengue virus sero types (DENV-1, 2, 3 & 4).[5] The diagnosis is based on history, clinical features and laboratory parameters. The Dengue virus infection can present as undifferentiated fever, dengue fever(DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). Though Most of the infections of mild,DHF mortality can reach upto 20 % if timely and proper treatment is not instituted.[6,7]

Major epidemic in Pakistan first occurred in Karachi in 1994,1995.[8] Dengue epidemics have occurred every year and has extended to most cities in Pakistan.[9] The number of patients suffering from Dengue Fever in the country increased from 21,204 patients in 2010 to 47,120 in 2018.[10] Dengue fever has become a significant health problem in Pakistan,Brazil and India due to increasing number of infections.[11]

The objective of this study isto assess the clinical, laboratory, radiological profile, management and outcome in children upto 12 years of age presenting with dengue infection to Pediatric department of Benazir Bhutto Hospital during 2019 outbreak.

Material and Methods

This prospective descriptive study was conducted at Department of Pediatrics, Benazir Bhutto hospital Rawalpindi, for period of 6 months from July to December 2019. One month to 12 years old children presenting with clinical features and symptoms of dengue infection who were admitted in the Pediatric ward were tested for NS1 antigen and IgM and IgG dengue antibody (depending on day of fever) by ELISA method. Those positive for NS1, IgM or both were included in the study. Patient age more than 12 years or suffering from previous known blood disorders were excluded. The diagnosis of dengue fever was based on the WHO criteria.

Clinical dengue fever was defined as fever 2-10 days of duration (essential criteria) with any two of the following:-

- Aches and Pain
- Irritability
- Rash
- Nausea and Vomiting
- Haemorrhagic manifestations
- Throbocytopenia

Dengue Hemorrhagic Fever (DHF) is defined by the following four criteria:

- Fever or recent history of fever lasting 2–10 days.
- Any hemorrhagic manifestation.
- Thrombocytopenia (platelet count of <100,000/mm3).
- Evidence of increased vascular permeability.

Dengue shock syndrome (DSS) is defined as having all of the four criteria of DHF plus evidence of circulatory failure manifested by

- Rapid, weak pulse
- Narrow pulse pressure < 20
- Capillary refilling time >2sec
- Hypotension for Age
- Cold clammy skin and restlessness

Prior approval from the hospital ethics committee was obtained. All this data was recorded and entered in the predesigned, pre-tested, and semi structured questionnaire. The relevant data was recorded, entered and analyzed by SPSS version 24 for descriptive statistics and bi-variate analysis.

Results

In the 6 months period of study, 438 dengue NS1/serology positive children were admitted, 254 were male children (58%), and 184 were female children (42%). The age of the children ranged from 03 months to 12 years, with a mean age of 8.13 years (SD ±3.4 years). Fever was the most common symptom observed in all children (100%). The time interval between the onset of fever and the day of admission varied from less than 24 hours to 8 days. The mean duration of fever on admission was three days.

Table 1: Age and Gender

Demography of Dengue Patients		
Gender	**Frequency(n= 438)**	**Percentage**
Male	254	58
Female	184	42
Less than 1 year	15	3.4
1-4 years	78	17.8
5- 8 years	114	26.1
9-12 years	231	52.7

The other common complaints were pain and aches 79.4% (348/438), decreased appetite 63.4% (278/438), vomiting 54.5% (239/438), and abdominal pain 39.3% (172/438). Other less common symptoms included skin rash, (transient macular, generalized rash and/or generalized morbilli-form maculopapular rash) was observed in 23.9% children. Decreased pulse pressure with increased capillary refilling time (CRT) was seen in 14.9% cases. Bleeding tendencies which included petechiae, purpura, epistaxis, and malena were present in 38.6%. Five children (1.2%) presented with convulsion on admission but none were dengue encephalitis/ encephalopathy.

Out of the total 438 children, 254 children were reported as uncomplicated dengue fever,119 children had dengue hamorrahgic, and 65 had dengue circulatory shock syndrome. Loss of appetite, abdominal pain, bleeding tendencies, Hypotensionn,narrowing pulse pressure and prolonged capillary refill time ($p<0.05$) were seen significantly associated with progression of disease and development of complication. In investigations, leucopenia 285 (65.1%) was the predominant

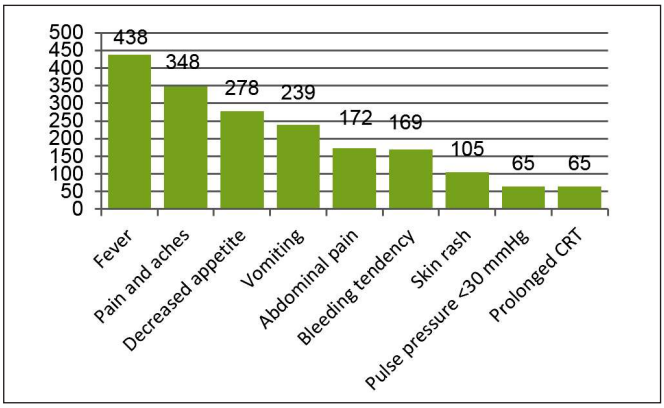

Fig 1. Clinical presentation

finding. A low platelets count (platelet count less than 100,000) was seen in 275 (62.7%) cases. Amongst the liver enzymes, ALT was deranged in a larger proportion (42%) of patients when compared to AST which was elevated in (27.85%). Ultrasound of the abdomen detected Abdominal / Pelvis fluid

Table 2: Significant clinical manifestations for development of Complications

Parameter	Variable	Dengue Fever N= 254	DHF N= 119	DSS N=65	P-Value
Fever	Present	254	119	65	
	Absent	0	0	0	
Vomiting	Present	101	87	51	0.001
	Absent	153	32	14	
Decreased Appetite	Present	174	60	44	0.002
	Absent	80	59	21	
Abdominal Pain	Present	44	81	65	0.001
	Absent	210	38	0	
Pain and Aches	Present	198	98	52	0.614
	Absent	56	21	13	
Skin Rash	Present	77	22	18	0.048
	Absent	177	97	47	
Bleeding Tendencies	Present	03	7	24	0.001
	Absent	251	42	41	
Pulse Pressure	>30	254	119	0	0.001
	<30	0	0	65	
Capillary Refilling Time	<2sec	254	119	0	0.001
	Prolonged	0	0	65	

40% of the cases, which is the most common finding followed by gall bladder wall edema in 63 children. Hepaomegaly and Splenomegaly were seen in 21% and 5.4 % cases respectively. 70.3% of the patients were NS1 positive while IgG ang IgM were positive in 62.1% and 14.8% respectively.Co-infection with enteric fever was seen in 30 children.

Thrombocytopenia, Leukopenia, HCT > 20% with platelets <50,000, deranged LFTs, Hyponatremia, Hepato-spleenomegaly and Gall bladder wall thickness on ultrasonography were seen significantly associated with progression of disease and development of complications. All patients were managed according to revised DEAG (Dengue Expert Advisory Group) guidelines 2019. Blood transfusion was needed in 6 (9.2%) cases with Dengue Shock Syndrome, while FFPs were administered to three children suffering from DHF.

Out of total 438 cases 254 children were reported as uncomplicated dengue fever. 119 children developed dengue hemorrhagic fever and were managed accordingly. 65 children went into dengue shock syndrome. One male child with DSS

Table 3: Laboratory and Radiological Features of Patients.

Blood Picture	Frequency	Percentage
Thrombocytopenia (platelets count <100,000)	275	62.7
Leukopenia (TLC < 4000)	285	65.1
Anemia (Heamoglobin<10)	99	22.7
HCT > 20% with platelet count<50,000	97	22
Dengue Serology		
NS1 Ag Positive	308	70.3
Dengue IgM	272	62.1
Dengue IgG	65	14.8
Dengue IgM positive with NS1 negative	97	22.1
Biochemistry		
Deranged LFT(ALT/AST)	306	69.8
Deranged RFT	15	8.1
Hyponatremia	95	51.7
Radiology		
USG findings Abdominal / Pelvis fluid	175	40
USG findings of gall bladder wall edema	63	14
USG findings of Hepatomegaly	95	21
USG findings of Splenomegaly	24	5.4

Table 4: Significant Laboratory Parameters for Development of Complications

Parameter	Variable	DF N= 254	DHF N= 119	DSS N=65	P-Value
TLC	< 4000	165	77	43	
	4000 -10000	83	37	20	0.991
	>10000	06	05	02	
Platelets	<100,000	98	112	65	0.001
ALT	<100	234	89	40	
	100-1000	20	29	21	0.000
	>1000	00	01	04	
HCT	>35	249	101	57	0.002
	<35	05	18	08	
USG	abdominal / pelvic fluid	0	110	65	
	Gall bladder wall edema	0	41	22	--
	hepatomegaly	0	30	65	
	splenomegaly	0	11	13	
Dengue Serology	NS1	149	102	57	
	IgM	146	99	27	
	IgG	13	28	24	0.000
	NS1+IgM	14	50	33	
	IgM + IgG	11	08	12	

died due to multi organ failure. Average duration of hospital stay remained 2.5 days (±1.2) for uncomplicated dengue fever, 4.9 (±1.9) days for dengue hemorrhagic fever while 7.3(±2.8) days for dengue shock syndrome.

Discussions

In tropical countries Dengue infection constitutes an important arboviral infection. Dengue virus infection can be associated with broad range of clinical presentations from an inapparent infection,mild fever to severe Dengue Shock syndrome which can be fatal.[12] WHO has classified Dengue infection into dengue fever, dengue hemorrhagic fever and dengue shock syndrome.[13] In our study, out of 438 cases, 254 children (58%) were reported as uncomplicated dengue fever. 119 children (40%) developed dengue hemorrhagic fever and were managed accordingly. 65 children (15%) went into dengue shock syndrome. Shubhankar Mishra et al, hasreported a similar percentage of severe dengue in 13.4% of the patients.[14]

Most of the infected children were of 8-12 years of age.similar age group has been reported in other studies.[11,12] Boys were more commonly affected than girls with male to female ratio of 1.2:1. This may be due to more out door activity of male and older children making them prone to mosquito bite.[15] In our study, like most other studies, fever was present in all the cases, on analyzing warning signs, reluctance to feed, vomiting, abdominal pain, pain and aches and bleeding tendencies were seen commonly.

In our study, we found rash in 23.9% cases. In a study of 300 patients by Nadia A *et al*,[16] maculopapular rash was present in 28.7%. In a study of 62 patients in Japan, by Itoda *et al*,[17] rash was more frequent in 82% cases. In a north Indian study by Karoli R *et al*,[18] rash was present in 26% cases while 16% had cutaneous hypersensitivity. Rahim MA *et al*, also found rash in high frequency of 78.5% in a Bangladesh based study.[19]

Thrombocytopenia (platelet count less than 1,00,000) was observed in 62.7% children in our study while bleeding manifestations were observed in 38.6% children.In a study by S Sahana *et al*, 82.7% patients had thrombocytopenia.[20] A Delhi based study by Tripathy BK *et al*, hematemesis, melena and epistaxis were found in 28.28%, 26.78% and 14.28% respectively but only 12.85% caseshad platelet count <70,000/cmm.[21] A Studyconducted on 84 cases in Sudan by Ageep AK *et al* bleeding was present in 93% of cases andthrombocytopenia in 88% cases.[22] Shubhankar Mishra *et al*, study reported 27.85% with thrombocytopenia where as Deshwal R *et al* reported 69.51% patients with thrombocytopenia. In our study, concomitant presence of leucopenia, raised haematocrit and low platelet count was commonly associated with dengue fever with warning signs. Decreasing sequential leukocyte count with increasing haematocrit and decreasing platelet count were reliable indicators of developing complications.

In our study, liver enzymes were in the range of 200 – 1000U/L, 3 patients had a value more than 1000 U/L.A raised transaminase level to fulminant hepatic failure can occur in dengue infection.[23]

In dengue serology, 308 were NS1 positive, 272 were IgM positive and 65 were IgG positive indicating secondary infection. Because all were sick on admission NS1 and IgM tests were done. NS1 antigen detection (70.3%) was found to be reliable and sensitive early indicator of dengue infection. All patients were managed according to revised DEAG guidelines 2019. Blood transfusion was needed in 6 (9.2%) patients withDSS, while FFPs were administered to three children suffering from DHF. One male child with DSS died due to multi organ failure.

Conclusion

The results of this study will help the policy makers, health professionals and other stakeholders in better understanding the situation of Dengue fever. Children in the age group of 8-12years were more commonly affected by dengue infection

with male predominance. Signs of plasma leak were found to be reliable indicators of the severity of disease helping in early institution of fluid therapy according to WHO guidelines, resulting in favorable outcome. Laboratory parameters like leukopenia, raised haematocrit and thrombocytopenia along with raised AST were strongly associated with risk of developing complications. Careful monitoring, early recognition of severe manifestation and timely intervention can reduce disease specific morbidity and mortality.

References

1. World Health Organization. https: //www.who.int/en/news-room/fact-sheets/detail/dengue-and-severe-dengue assessed 24.12.2019
2. Division of Vector Borne Infectious Disease. Dengue Fever. Atlanta, Ga: Centers for Disease Control and Prevention; 2008
3. Promprou S, Jaroensutasinee M, Jaroensutasinee K. Climatic factors affecting dengue hemorrhagic fever: incidence in southern Thailand. *Dengue Bulletin* 2005;29
4. Ali J. Dengue fever: symptoms, treatments and prevention; a general perspective. *World J Zool* 2015: 10(1): 22-5.
5. Shanthi G, Rajarajan S. A study on in vitro screening of antiviral activity of lyophilized extracts of three medicinal plants on dengue 2 & 4 serotypes. *Int J Recent Sci Res* 2014; 5(4): 740-4
6. Choudhury J, Shastri DD. Diagnosis and management of dengue in children: Recommendations and IAP ID chapter plan of action. *Pediatr Infect Dis* 2014;6(2):54- 62.
7. Kabilan L, Balasubramanian S, Keshava SM, *et al*. The 2001 dengue epidemic in Chennai. *Indian J Pediatr* 2005;72(11):919-23.
8. Special Programme for Research, Training in Tropical Diseases, and World Health Organization, Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control, World Health Organization, Geneva,Switzerland, 2009.
9. Rasheed SB, Butlin RK, Boots M. A review of dengue as an emerging disease in Pakistan. Public health. 2013 Jan 1;127(1):11-7.
10. World Health Organization. WHO report on global surveillance of Epidemic prone infectious diseases.http://apps.who.int/iris/bitstream/10665/66485/1/WHO CDS CSR ISR 2000.1.pdf.
11. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, *et al*. The global distribution and burden of dengue. *Nature* 2013;496(7446):504-7.
12. Endy TP, Anderson KB, Nisalak A, Yoon IK, Green S, Rothman AL, *et al*. Determinants of unapparent and symptomatic dengue infection in a prospective study of primary school children in Kamphaeng Phet, Thailand. *PLoSNegl Trop Dis* 2011;5(3):e975.
13. Deen JL, Harris E, Wills B, Balmaseda A, Hammond SN, Rocha C, *et al*. The WHO dengue classification and case definitions: time for a reassessment. *Lancet* 2006;368(9530):170-3.
14. Mishra S, Ramanathan R, Agarwalla SK. Clinical profile of dengue fever in children: A study from Southern Odisha, India. Scientifica. 2016 Apr 24;2016
15. Sajid A, Ikram A, Ahmed M. Dengue fever outbreak 2011: clinical profile of children presenting at Madina teaching hospital Faisalabad. Journal of University Medical & Dental College. 2012;3(1):42-7.
16. Nadia A. Malik M, Jamil A. Jahangir M. Cutaneous manifestations in patients of dengue fever. *J Pakistan Assoc Dermatologists* 2012; 22(4):320-4.
17. Itoda I, Masuda G, Suganuma A, Imamura A, Ajisawa A, Yamada KI, *et al*. Clinical features of 62 imported cases of dengue fever in Japan. *Am J Trop Med Hyg* 2006;75(3):470-4.
18. Karoli R, Fatima J, Siddiqi Z, Kazmi KI, Sultania AR. Clinical profile of dengue infection at a teaching hospital in North India. *J Infect Dev Ctries*. 2012;6(7):551–4.
19. Rahim MA, Sikder MS. Clinicopathologic manifestations and outcome of dengue fever and dengue haemorrhagic fever. *Bangladesh Med Res Counc Bull* 2005;31(1):36-45.
20. Sahana KS, Sujatha R. Clinical profile of dengue among children according to revised WHO classification:analysis of a 2012 outbreak from Southern India. *Indian J Pediatr* 2015;82(2):109-13
21. Tripathi BK, Gupta B, Sinha RSK, Prasad S, Sharma DK. Experience in adult population in dengue outbreak in Delhi. *J Assoc Physicians India* 1998;46(3):273-6
22. Ageep AK, Malik AA, Elkarsani MS. Clinical presentations and laboratory findings in suspected cases of dengue virus. *Saudi Med J* 2006; 27(11):1711-3.
23. Samanta J, Sharma V. Dengue and its effects on liver. *World J Clinical Cases* (WJCC) 2015 Feb 2;3(2):125.