Original Research Article

Clinical profile and outcome of children admitted for dengue with warning signs and severe dengue

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Abstract

Objective: To study clinical profile and outcome of children with dengue with warning signs and severe dengue. **Design**: Prospective observational study over period of one year. **Subjects and methods**: Ninety five children diagnosed as dengue with one or more warning signs on presentation or with severe dengue features were enrolled .Those suffering from dengue fever but without warning signs were excluded from study. Their clinical features, serial hematological and other investigations were noted. Fluid therapy and other supportive treatment was done according to WHO and IAP infectious disease chapter guidelines. The outcome was assessed in terms of course in hospital. **Results:** Total 95 children were enrolled, 67 with dengue warning signs and 28 with severe dengue. Common warning signs were abdominal pain/tenderness, liver enlargement, lethargy and restlessness. Those with severe dengue had respiratory insufficiency due to acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), refractory shock and severe bleeding. Two presented with dengue encephalitis. Of 95 children enrolled in study 7 (7.36%) died. Case fatality rate was more (21.4%) in those who presented with severe dengue compared with those who presented with warning signs (1.4%). **Conclusion**: Dengue is one of the dreaded fevers of pediatric age group. Dengue has variable clinical presentation. But, timely picking up cases with set of warning signs given by WHO in critical phase of illness followed by stepwise protocol based fluid therapy can reduce case fatality.

Key Words: Dengue fever, dengue warning signs, severe dengue, dengue WHO guidelines.

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INTRODUCTION

Dengue is the fastest emerging arboviral infection spread by Aedes mosquitoes with major public health consequences in over 100 tropical and subtropical countries including Southeast Asia. About 2.5%of those affected with dengue die of the disease[1]. Children are at higher risk of acquiring severe Dengue. Epidemological studies conducted in India during dengue epidemic have shown that dengue hemorrhagic fever has been predominantly restricted to children[2,3]. In 2009, WHO revised classification for Dengue in to dengue fever with or without warning sign and severedengue[4]. The new classification encompasses a set of 'warning signs' intended to help clinicians identify patients likely to develop complications during critical phase of illness. This early picking up of case with warning signs and treating them according to fluid therapy protocol[5,6] has resulted in decrease in mortality. Current prospective observational study was carried out to know clinical profile and outcome of children with dengue warning signs and with severe dengue.

MATERIALA AND METHODS

This study was conducted at tertiary care hospital at Aurangabad (MS) from 1st jan2015 to 31st Dec 2015 .This is prospective observational study of children admitted for dengue with warning sign and those who are presented with severe dengue. There clinical profile, laboratory investigation and clinical course and outcome was noted.

Warning Signs in Dengue[4]

1. Abdominal Pain /tenderness
2. Persistent Vomiting
3. Clinical fluid accumulation
4. Mucosal bleed
5. Lethargy, Restless
6. Liver enlargement>2cm
7. Increases in hematocrit with concordance rapid decrease in platelets

Criteria for Severe Dengue[4]

1. Severe plasma leakage leading to dengue shock syndrome (DSS)
2. Fluid accumulation with respiratory distress
3. Severe bleeding
4. Severe organ impairment
5. Liver ALT or AST >1000
6. CNS -Altered consciousness

Inclusion Criteria

Children (age group 0-15 years) suffering from dengue fever and who presented with one or more warning sign or as severe dengue were enrolled. Cases with typical clinical features and laboratory investigations supported by positive serology (dengue IgG,IgM by Eliza method) were included as dengue case. Children suffering from dengue fever but without warning sign or features of severe dengue were excluded from study. They were admitted in pediatric ICU and monitored by laboratory investigations and repeated focused clinical examination and monitoring. Laboratory parameters studied were CBC, hematocrit, coagulation profile, ABG, CXR, USG abdomen and 2D-ECHO if needed. Management was done according to current WHO guidelines (5) and IAP recommendation and guidelines on management of dengue fever in children (6).

OBSERVATIONS AND RESULTS

Total 95 subjects with dengue warning sign (one or more) or severe dengue features were included for study. Out of 95, 68(71.5%) were male and 27(28.4%) were female. Thirty nine (41.05%) children were from rural area and 56 were from urban area (58.9%).Month wise distribution of cases was noted. Maximum cases were recorded in October (32 i.e.33.6%) followed by November (23 i.e. 24.2%).From January to May there were only 2 cases. Average duration of stay was 7 while average duration of intravenous fluid requirement was 3.9days. Seventy children (73.68%) patient were above 8 year of age while 26 children (26.3%) were <8year of age. Sixty seven (70.5%) patient were having one or more warning signs while 28(29.4%) had severe dengue features. Sixty seven (70.5%) cases included had one or more warning signs as follows (table no 1).

Table 1: Dengue with warning signs

Sr. No.	Warning sign	No of cases	Percentage
1.	Abdominal pain /tenderness	67	100%
2.	Increase in haematocrit with concurrent rapid decrease in platelets	50	74.6%
3.	Persistent vomiting	10	14.9%
4.	Clinical fluid accumulation	48	71.6%
5.	Liver enlargement >2cm	57	85%
6.	Lethargy/restless	54	80.5%

Severe dengue Twenty eight (29.4%) included had severe dengue features on admission .Their presentation was as follows.

Table 2:

Sr No.	Severe dengue feature	No of cases	Percentage
1	Refractory shock	7	25%
2	Respiratory distress with acute lung injury	12	42.8%
3	Respiratory distress with ARDS	3	10.7%
4	Severe bleeding	4	14.28%
5	Dengue Encephalitis	02	7.1%

Other findings Leukopenia was observed in 82 (86%).Increased SGPT>100 was observed in 84 (88%) cases. Blood products were needed in 40 (42.1%) cases. Furosemide infusion was needed in 14 (14.73%) cases. Ventilatory support was needed in 28 (29.4%) cases.

Outcome

Among 95 children enrolled in study 7 died .Case fatality rate was 7.36%. However significant difference in mortality was noted in cases who presented with one or more warning signs and those who presented with severe dengue features. Among 28 cases who presented with severe dengue 6 (21.4%) died. From remaining 67 cases of dengue who presented with warning sign only 1(1.4%) died. All cases that died had refractory shock and multiorgan failure .One case who presented with dengue encephalitis subsequently had refractory shock and multiorgan failure and died.

DISSCUSSION

Dengue remains puzzling disease in many areas like variability of presentation and host virus relationship. At time it behaves like a simple self-limiting febrile illness while at time it leads to mortality. In South East Asia region, number of dengue cases had increasedover last few years with recurring epidemics .Also there has been increase in proportion of dengue cases with more severity.[1] In Present study, males were more affected (71.5%) compared with females (28.4%).Similar observation has been noted by some authors[7]. There was higher incidence in older age group >8years (73.68%).Similar observation was noted by previous studies[8,9]. There were significant cases from rural area (41.05%).Dengue is no longer restricted to urban centers, with outbreaks occurring in rural India .Nearly every state of India including island such as Andaman and Nicobar now reports cases[6]. A seasonal pattern was observed. Majority cases (86.31%) were in four months from August to November .These month sconstitutes monsoon and post monsoon season in India. This is due to increased mosquito breeding due to availability of water in this season .Similar seasonal pattern has been observed by many authors[8,10]. After incubation period, dengue illness abruptly beginsin phases i.e. febrile phase, critical phase and recovery phase. Most patients demonstrate the characteristic biphasic temperature pattern[11]. In present study, only dengue cases with one or more warning sign at presentation or presenting as severe dengue were included, so all were in second i.e. critical phase of illness. The 1997 WHO guidelines classified dengue into dengue fever /dengue hemorrhagic fever (grade 1and 2) and dengue shock syndrome (grade3and 4)[12]. Experience with this classification system has exposed number of limitations[13]. The international Denco study was designed to evaluate the perceived limitations of 1997 criteria in South East Asia and Latin America to develop evidence based classification that would better reflect clinical severity[14]. These results formed the basis of the revised 2009 WHO classification system. Current study was undertaken to look into outcome of dengue with warning sign and severe dengue according to new classification system. In current study 67 (70.5%) cases had one or more warning signs on admission .The most common presentation was abdominal pain/tenderness which was seen in all cases (100%).Similar observation were recorded by other authors.[15] This concludes that abdominal pain in critical phase of dengueillness should be given significance and child should be admitted and monitored. Increased hematocrit was noted in only 50%cases with warning signs, although concurrent rapid drop in platelet count was seen in all (100%) cases. It may be due to high prevalence of anemia in this region. Gomber *et al* in their study defined the cut-off hematocrit value of 36.3% in 6-12 years of age group as diagnostic of dengue hemorrhagic fever[16]. A study from Chennai by Balsubramania *et al* showed hematocrit value of 34.8%in <5yars and 37.5%in >5years of age as good predictors of hemoconcentration in DHF[17]. Clinical fluid accumulation due to capillary leak not causing respiratory compromise was seen in 71.6%cases with warning signs while 42.8%cases who presented with sever dengue had fluid accumulation with respiratory compromise. Jain H observed clinical fluid accumulation in form of ascites and pleural effusion with reduced air entry in 40% and 43%of cases respectively[15]. Liver enlargement (> 2 cm) was found to be another common warning sign seen in 85% cases. Similar finding were noted by Siddharth Bhave *et al*[8] and Ratageri *et al*[18]. Restlessness and or lethargy were common presenting warning signs observed in 80.5%cases.Ratageri *et al* observed restlessness in 65%cases in their study[18]. We noted that those who presented with restlessness and or lethargy had shock and hypoxia so has to be treated in PICU urgently. Of 28 cases who presented with severe dengue, 12(42.8%)patients had acute lung injury(ALI) while 3(10.7%)had acute respiratory distress syndrome (ARDS).Consensus definition given by Wheeper *et al*[19] was used for ALI and ARDS case definition. Disruption of alveolar capillary barrier in ALI and ARDS results in increased permeability, influx of protein rich edema fluid in alveolar sac, dysfunction of surfactant function. They all needed Ventilatory support for treatment. Dengue complicated by ARDS has high mortality as noted by previous authors[20,21]. Four of 28 cases with severe dengue had severe bleeding in form of hematemesis. Cause of bleeding in severe is multifactorial i.e. deranged liver function, hypoxia, and metabolic acidosis along with low platelets leads to coagulation failure. There was poor correlation between level of low platelet count and severity of bleeding manifestations. Similar observations had been noted by other authors[8,20]. There were two cases from severe dengue group who presented as dengue encephalitis. Dengue virus is not classically neurotropic virus, although there is recent evidence of direct neuronal injury. The serotypes most frequently implicated in causing neurological manifestations are DEN 2 and DEN3[22]. Encephalopathy is very common neurological complication of dengue which is usually secondary to multisystem derangement like shock, liver dysfunction, coagulopathy and concurrent bacterial infection[23]. Dengue encephalitis is a different entity which occurs due to direct neuronal infiltration of dengue virus[22,24]. Case definition criteria described by Varathraj A was used to define dengue encephalitis[25]. They had fever, headache, altered sensorium, seizures which were not explained by

presence of any liver, kidney or electrolyte derangement. One child with dengue encephalitis improved fully without neurological sequelae. Other one died as he progressed to refractory shock and multiorgan failure. Cases of dengue encephalitis has been reported by other author[26]. Six cases (21.4%) among 28 with severe dengue had refractory shock. They all came late in course of illness and from remote areas without proper fluid resuscitation. Patients with severe plasma leakage may not have shock if prompt fluid replacement has been carried out. Prolonged hypotensive shock and hypoxia lead to severe metabolic acidosis, multiple organ failure and extremely difficult clinical course[6]. One child presented with Dengue encephalitis but subsequently had refractory shock and died. In present study, case fatality rate was 7.36%.Mortalty was more (21.4%)in severe dengue group compared with dengue with one or more warning sign group(1.4%).This highlights importance of early recognition of warning signs with proper treatment according to standard protocol[5,6]. All case with refractory shock had narrow pulse pressure. WHO has used lowered systolic blood pressure or narrow pulse pressure as criteria to classify dengue in different severity grade[12]. Similar findings has been observed by other clinicians[27]. Late presentation to hospital has been identified as independent predictor of severe disease[28]. This highlights importance of fluid resuscitation in compensated shock. So if patient receives proper care in warning phase of illness progression to refractory shock and multiorgan failure can be avoided.

CONCLUSION

Dengue is one of the dreaded fevers of pediatric age group. Dengue has variable clinical presentation. But, timely picking up cases with set of warning signs given by WHO in critical phase of illness followed by stepwise protocol based fluid therapy can reduce case fatality.

REFERENCES

1. World health organization. Comprehensive guidelines for prevention and control of dengue haemorrghic fever. Revised and expanded edition. SEARO technical publication series no 60.WHO, 2011.
2. Kamath SR. Ranjit S. Clinicalfeatures, complications and atypical manifestations of children with severe form of dengue hemorrhagic fever in South India. Indian J Pediatr 2006; 73(10)889-95.
3. Narayan M, Aravind MA, Thilothammal N, Prerna R, Sargunam CS, Ramamurthy Dengue fever epidemic in Chennai: a study of clinical profile and outcome. Indian Pediatr 2002; 39(11)1027-33.
4. World health organization. Dengue: Guidelines for diagnosis, treatment, prevention and control. Geneva, Switzerland: WHO, 2009.
5. World health organization. Handbook for clinical management of Dengue. Geneva, Switzerland: WHO, 2012.
6. Jaydeep Chowdhary, Digant Shastri. Diagnosis and management of dengue in children: Recommendations and IAP ID chapter plan of action. Pediatric infectious disease,6(2014):54-62.
7. Sahana KS, Sujatha R. Clinical profile of dengue among children according to revised WHO classification: analysis of 2012 outbreak from Southern India. Indian J Pediatr 2015;82:109-13.
8. Bhave S, Rajput CS, Bhave S .Clinical profile and outcome of dengue fever and dengue haemorrghic fever in Pediatric age group with special reference to WHO guidelines(2012)on fluid management of dengue fever. International Journal of advanced research 2015,vol-3, issue 4,196-201.
9. Agrawal R, Kapoor S, Nagar R, et al. A clinical study of patients with dengue haemorraghic fever during the epidemic of 1996 at Lukhnow. South East Asian J Trop Med Health1999.30 (4); 735-41.
10. Wongkoon S, Jaroensutasinee M, Jaroensutasinee K. Distribution, seasonal variation and dengue transmission prediction in Sisaket, Thailand. Indian J Med Res 2013.138(3):347-353.
11. Scott B, Halsteed. Nelson textbook of Paediatrics,20th edition.Elsevier,Philadelphia.2011:1629-32.
12. WHO. Dengue hemorrhagic fever: Diagnosis, treatment, prevention and control.2nd edition. Geneva, Switzerland: WHO,1997.
13. Rezeki s Hadinegoro. The revised WHO dengue classification: does the system need to be modified? Pediatrics and international child health 2012,vol 32:33-37.
14. Alexander N, Badmaseda A, Coelho IC, Dimaano E, Hien TT, Hung TT. Multicenter prospective study on dengue classification in four South east Asian and three Latin America countries. Trop Med Int Health 2011;vol 16 no 8:936-48.
15. Jain H. Clinical profile and outcome of dengue fever in hospitalized children of South Rajasthan, India. Int J contempPediatr2016; 3(20:546-49.
16. Gomber S. Ramachandran VG, Kumar S, et al. Hematological observations as diagnostic markers in DHF-A reappraisal. Indian Pediatr 2001;38:477-81.
17. Balasubramanian S, Anandathan K, Shivabalam S, Dutta M, Amalrej E. Cut off hematocrit value for hemoconcentration in dengue hemorraghic fever. J trop Pediatr 2004;50:123-24.
18. RategiriVinod H, ShepurTA, Wari PK, ChavanSC, MujahidI B, Yergolkar PN. Clinical profile and outcome of dengue fever cases. Indian J Pediatr2005;72(8):705-6.
19. Wheeper AP, Bernard GR. Acute lung injury and acute respiratory distress syndrome:a clinical review. Lancet 2007,369;1553-64.
20. Dhooria G, Bhat D, Bains H. Clinical profile and outcome in children of dengue haemorrghic fever in North India. Iran J Pediatr. Sep 2008;vol 18(no 3):222-28.
21. LumLC, Thong MK, Cheah Y ketal. Dengue associated adult respiratory distress syndrome. Ann Trop Pediatr 1995;15(4):335-39.

22. Solomon T, Dung NM, Vaughn DW, Kneen R, Thao Lt, Raengsakulrach B et al. Neurological manifestations of dengue infection. Lancet 2000; 355:1053-9.
23. Koley TK, Jains, Sharma H, Kumar S, Mishra S, Gupta MD et al. Dengue encephalitis. Jassoc Physicians India.2003;51:422-23.
24. Nathanson N, Cole GA. Immunosuppression and experimental virus infection of the nervous system. Adv Virus Res.1070;16:397-428.
25. Varathraj A. Encephalitis in the clinical spectrum of dengue infection. Neurol India.2010; 58:585-95.
26. Arora S, Agrawal A, Mittal H. Dengue encephalitis in children. J Neurosci Rural Pract 2012 May-Aug;3(2)228-29.
27. Morens DM, Fauci AS. Dengue and dengue haemorrghic fever; a potential threat to public health in the United States. JAMA 2008;299(2):214-16.
28. Jain S, Mittal A, Sharma SK et al. Predictors of dengue related mortality and disease severity in a tertiary care center in North India. Open forum infectious diseases major article;2017.DOI:10.1093/ofid/ofx056.

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