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Research Article

CLINICAL AUDIT OF FLUID THERAPY IN DENGUE FEVER WITH REFERENCE TO SEVERITY OF PRESENTATION AND COMPLICATION

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ABSTRACT

Introduction: Dengue fever is an acute febrile infectious disease presenting with capillary leak. Fluid replacement during critical phase is based on clinical symptoms, signs, laboratory investigation and urine output, which is the main stay of treatment. Over/ under correction of fluid during critical phase have its own consequences. Hence the present study is undertaken to audit the fluids administered vide the national guidelines in correlation to the Srilankan guideline and evaluate the complications. *Material & Methods:* A hospital based prospective observational study was conducted at Department of Paediatrics, MVJ Medical College & Research Hospital. A total of 100 consecutive children with dengue fever, fulfilling the eligibility criteria were included. Fluid resuscitation was started as per the National guidelines of 2014 and correlated with Srilankan guidelines. Complication due to overload/underload due to fluid administration was noted. *Results:* Of the 100 children, 82 were dengue with warning signs and 18 were severe dengue. Mean hematocrit and liver function derangement was significantly higher and mean leukocyte and platelet count were significantly lesser in patient with severe dengue. All 82 patients (100%) of dengue with warning signs needed lower crystalloid fluid rate of 5ml/kg/hr and 3 ml/kg/hr for a mean duration of 14.5 hours and 28 hours respectively in addition to ORS. Higher fluid rate like boluses, 10 ml/kg/hr and 7 ml/kg/hr were required in patients with severe dengue during first 12 hours after admission. None of the patients were noted to have fluid under correction. 5 out of 18 patients in severe dengue who expired required higher fluid rates and boluses of crystalloid and colloids and their fluid quota was >150 ml/kg, during the critical phase as against Srilankan guidelines. Complications like profound shock in 3 patients (16.5%) and death due to ARDS in all these 5 patients (27.8 %) of severe dengue was observed within 9 to 11 hours of admission. *Conclusion:* 95 % of patients recovered by following National guidelines of fluid therapy. However in 5 %, it was associated with fluid overload and complication like ARDS and death.

Keywords: *Dengue fever, IV fluids, Complication*

INTRODUCTION

Dengue is the most widely distributed mosquito-borne viral infection of humans, affecting an estimated 50 million people worldwide each year with 30 fold increase in last 50 years. There are 4 serotypes of dengue virus, all of which may produce either a nonspecific febrile illness, dengue fever (DF) or may result in the more severe manifestation of Dengue Hemorrhagic Fever.

The pathophysiology of DHF is not clear, but the main feature differentiating it from DF is an increase in vascular permeability, resulting in leakage of fluid from the intravascular compartment to the extravascular space.Narrowing of the pulse pressure is recognized as one of the earliest manifestations of shock, and occurs before the development of hypotension. The mainstay of treatment is vigorous fluid resuscitation. If appropriate volume resuscitation is started at an early stage, shock is usually reversible; in very severe cases, and in those in whom the resuscitation is inadequate, patients may progress to irreversible shock and death. The commonly used fluids in the management of dengue fever include oral rehydration solutions (containing solutes), intravenous solutions such as crystalloids (isotonic fluid replacement) and colloids (plasma equivalents). In this context, the present study aims at studying the

audit of fluid in dengue fever with reference to severity of presentation and the complication resulting from fluid therapy.

Aim and Objectives

1. To audit the fluid therapy in dengue fever with reference to the severity at presentation based on WHO and Srilankan guidelines.
2. To study the over or under correction of fluid and its complication.

MATERIALS AND METHODS

Study Area

It was carried out in the Department of Paediatrics, MVJ Medical College & Research Hospital.

Study Population

The selection of patients for study was done as per WHO guidelines (2012) along with serological evidence in the form of positive Dengue NS1Ag and/or positive Dengue IgM. Patients were assessed for clinical manifestations, vital parameters like blood pressure, pulse rate, respiration, level of consciousness, hydration and bleeding tendency. The complications at any stage of dengue disease were recorded. The patients were subjected to routine laboratory tests like haemoglobin (Hb), total leukocyte count (TLC), Haematocrit, total platelet count, peripheral smear. Fluid resuscitation was instituted as per the National guidelines of 2014.

The clinical audit of fluid was based on following parameters:

- Clinical parameter at a given point and evaluate, does it match the fluid recommended.
- Whether fluid recommended in the previous hour has been given for the patient on hourly basis and correlate it with clinical signs.
- Effect of quantity of fluid transfer over the period of capillary leak on a 24 hour basis on the clinical status of the patient.
- Correlate Srilankan guidelines with National guidelines.
- Complication due to overload/underload due to fluid administration.

Statistical analysis:

- General characteristics of the patients were expressed as values of mean and standard deviation for quantitative variables and percentages for qualitative variables
- Statistical analyses were performed using chi-square test for categorical variables and t-test for continuous variables. *p* values less than 0.05 will be considered significant.

Method of collection of Data:

Dengue cases of Paediatric age group during the period of November 2016 to October 2018 satisfying the inclusion criteria were included in the study.

Inclusion criteria:

- Children from 1 to 18 years of age with positive Ns1Ag and/or IgM as described in WHO 2012 criteria requiring fluid administration

Exclusion criteria*:*

- Children having co-morbid condition not directly attributed to disease.
- Children on medication likely to affect fluid homeostasis.
- Children requiring mechanical ventilation on admission.

RESULTS

100 children with dengue were studied. Of them 82 patients were dengue with warning signs (DWS) and 18 were severe dengue (SD) cases.

Characteristics of patients included in the study are represented in Table no. 1

Table no. 1: Characteristics of patients included in the study

	Dengue with warning signs (DWS)	Severe dengue (SD)	P value
Age			
<5 years	18	6	
6 to 10 years	37	8	0.633
11 to 15 years	24	4	
>15 years	3	0	
TOTAL	82	18	
Sex			
Female	33	9	0.448
Male	49	9	
Serology			
Ns1Ag positive	73	18	0.141
IgM positive	9	0	
Duration of Fever (mean days)	3.2±0.5	4.1±0.6	<0.001*
Clinical features			
A) Abdominal pain	74	18	0.167
B) Persistent Vomiting	68	18	0.059
C) Clinical fluid accumulation	50	17	0.006*
D) Mucosal bleeding	1	7	<0.001*
E) Lethargy	3	6	<0.001*
Clinical signs			
Pulse rate			
a) Normal	82	0	
b) Bradycardia	0	4	<0.001*
c) Tachycardia	0	14	
Peripheral Pulse			
a) Feeble	0	6	
b) Not felt	0	8	<0.001*
c) Well Felt	82	4	
Respiratory rate			
a) Normal	79	3	
b) Tachypnea	3	15	<0.001*
Sensorium			
a) Altered consciousness	0	6	<0.001*
b) Normal	82	12	

Urine output			
a) Normal	76	0	
b) Decreased	6	18	<0.001*
Abdominal girth			
a) static	66	0	
b) Increased	16	18	<0.001*
laboratory findings			
a) HB	10.79±1.59	11.68± 1.28	0.028*
b) Total count	6032.32± 1957.08	3470.56± 1193.41	<0.001*
c) Hematocrite	33.66± 4.42	38.94±3.81	<0.001*
d) Platelet count	92378.05±31835.47	34333.33±16761.30	<0.001*
e) PeripheralSmear			
a) Normal	74	1	<0.001*
b) Thrombocytopenia	8	17	
f) Liver function test			
a) Normal	64	0	<0.001*
b) Altered	18	18	
g) Renal function test			
a) Normal	81	12	<0.001*
b) Altered	1	6	
h) X Ray			
a) Normal	76	0	
b) Bilateral Pleural Effusion	0	10	<0.001*
c) Bilateral Pleural Effusion, Acute Respiratory Distress Syndrome	0	5	
d) Unilateral Pleural Effusion	6	3	

Difference in duration of fever, clinical signs and laboratory findings between dengue with warning signs and severe dengue were statistically significant.

Table 2: Comparison of IVF Rates between DWS and SD

		Diagnosis			
		DWS (n=82)		SD (n=18)	
		Count	%	Count	%
IVF Rate per hour	3 ml/kg	64	78.0%	0	0.0%
	3,5 ml/kg	6	7.3%	0	0.0%
	5,3 ml/kg	12	14.6%	0	0.0%
	7,5,3 ml/kg	0	0.0%	1	5.6%
	BOL,10 ml/kg	0	0.0%	3	16.7%
	10,7 ml/kg	0	0.0%	1	5.6%
	10,7,5,3ml/kg	0	0.0%	13	72.2%

16.7 % of severe dengue required bolus fluid therapy and all of severe dengue required higher fluid rates like 10 ml/kg/hr, 7 ml/kg/hr or 5 ml/kg/hr.

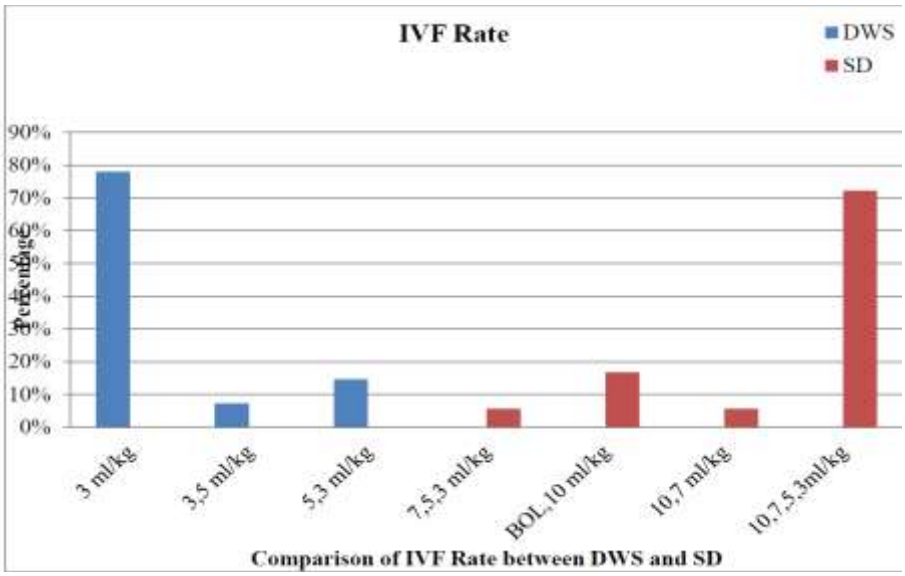

Table 3: Rate of IVF fluids and its duration in hrs

		IVF rate @ 3ml		IVF rate @ 5ml		IVF rate @ 7ml		IVF rate @ 10ml		Bolus	
		Count	%	Count	%	Count	%	Count	%	count	%
Duration in hrs	0-2	0	0%	0	0%	2	14.3%	12	70.6%	4	100 %
	3	0	0%	1	3.2%	5	35.7%	1	5.9%	0	0 %
	4	1	1.1%	3	9.7%	6	42.9%	0	0%	0	0%
	5	0	0%	0	0%	0	0%	3	17.6%	0	0%
	6	1	1.1%	6	19.4%	1	7.1%	0	0%	0	0%
	7	0	0%	0	0%	0	0%	1	5.9%	0	0%
	8	1	1.1%	2	6.5%	0	0%	0	0%	0	0%
	10	1	1.1%	6	19.4%	0	0%	0	0%	0	0%
	12	5	5.3%	9	29.0%	0	0%	0	0%	0	0%
	14	1	1.1%	1	3.2%	0	0%	0	0%	0	0%
	15	0	0%	1	3.2%	0	0%	0	0%	0	0%
	20	4	4.2%	0	0%	0	0%	0	0%	0	0%
	24	11	11.6%	1	3.2%	0	0%	0	0%	0	0%
	25	1	1.1%	0	0%	0	0%	0	0%	0	0%
	26	0	0%	1	3.2%	0	0%	0	0%	0	0%
	28	2	2.1%	0	0%	0	0%	0	0%	0	0%
	30	11	11.6%	0	0%	0	0%	0	0%	0	0%
	33	1	1.1%	0	0%	0	0%	0	0%	0	0%
	34	8	8.4%	0	0%	0	0%	0	0%	0	0%
	36	20	21.1%	0	0%	0	0%	0	0%	0	0%
	37	1	1.1%	0	0%	0	0%	0	0%	0	0%
	38	5	5.3%	0	0%	0	0%	0	0%	0	0%
	40	10	10.5%	0	0%	0	0%	0	0%	0	0%
	42	2	2.1%	0	0%	0	0%	0	0%	0	0%
	48	7	7.4%	0	0%	0	0%	0	0%	0	0%
	50	2	2.1%	0	0%	0	0%	0	0%	0	0%

Fluid bolus was required during first 2 hours of admission and higher fluid rates like 10 ml/kg and 7 ml/kg were required within first 6 hours of admission in dengue fever. Lower fluid rates like 5 ml/kg/hr and 3 ml/kg/hr were required for 8- 26 hrs after admission where as 3 ml/kg/hr was given from 28 - 50 hrs.

DISCUSSION

Dengue fever is becoming common in tropical countries like India due to climatic changes, urbanisation and inadequate waste management. While managing dengue fever, hourly observations and immediate access to haematocrit testing coupled with a conservative intervention policy allow fluid requirements to be met as early as possible and carefully titrating of fluid decreases complications like fluid overload. This study was under taken to audit fluid therapy clinically, in dengue fever with reference to severity of presentation and its complication.

The study was conducted over a period of two years from November 2016 to August 2018 on 100 confirmed Dengue cases of Paediatric age group of 1 to 18 years.

In this study, 45 % of dengue cases were aged between 6 to 10 years with male predominance (58%). In DWS 91 % of the patients were Ns1Ag positive, whereas in severe dengue all 100 % were Ns1Ag positive.Fever, abdominal pain and persistent vomiting are predominant symptoms in the present study. Patients in both severe dengue and dengue with warning signs have predominant symptoms of fever, abdominal pain and persistent vomiting. Thus these symptoms are not helpful in predicting the severity of dengue fever.Common clinical signs seen were hepatomegally, mucosal bleeding, lethargy and clinical fluid accumulation.Clinical signs like altered consciousness, hypotension, feeble pulse and tachypnea are significantly more common in patient with severe dengue in the present study. Hence we can conclude that altered consciousness, hypotension, feeble pulse and tachypnea are the significant markers for the severity of dengue. Hematological parameters are very helpful for disease monitoring and in prediction of prognosis.

In this present study, fluid therapy was given based on National guidelines of dengue management 2014. 100 patients were evaluated for the study andclassified based on WHO 2012 guidelines, 18 were severe dengue and 82 were denguewith warning signs. Fluid therapy was initiated based on clinical symptoms, signs, laboratory investigations and urine output of the patient. Intravenousfluids were given through flow regulator and carefully titrated based on hematocrite, urine output and clinical manifestation.

In the present study, mean duration of fever in dengue with warning signs is 3.2+ 0.5 days and in severe dengue 4.1+ 0.6 days. Severe dengue patients were admitted on 5th day of illness and these patients were already in critical phase of more than 24 hours. In these patients capillary leak had already started on admission. Hence more fluid was needed for the patient with severe dengue in comparison to patient with dengue with warning signs.

Higher fluid rate like boluses, 10 ml/kg/hr and 7 ml/kg/hr was given within first 12 hours in the study subjects whereas less fluid rates like 5 ml/kg/hr and 3 ml/kg/hr were given more frequently during 24 to 48 hours of admission. After the 48 hours since critical period is over, very few patients needed intravenous fluid. Hence early picking up of critical phase is crucial in administering fluid therapy indengue fever and also reducing intravenous fluid rate after they come out of criticalperiod is essential.

Srilankan guidelines of dengue management in 2012 suggest that one needs to be cautious of the fluid administered in patient with dengue fever. Total fluid given in critical phase of dengue fever shouldn't be more than maintenance + 5% dehydration, which is equivalent to 50ml/kg. For a 10 kg child, it will be 100ml/kg +50ml/kg, total of 150ml/kg in 24 hours. But in the present study majorityof patients of dengue with warning signs were successfully treated with 3 ml/kg/hr and 5 ml/kg/hr. Patients with severe dengue who expired required more intravenous fluid in critical phase, which was more than what Srilankan guidelines had suggested.

82 patients of dengue with warning signs received crystalloids fluid at 5 ml/kg/hr for a mean duration of 14.5 hours (3- 26 hrs) followed by 3 ml/kg/hr for mean duration of 28 hours (4-50) in addition to ORS.

None of these patients received crystalloid bolus or colloids. All of them recovered with intravenous fluids along with ORS given for a duration of 24 to 48 hours. None of these patients developed signs of fluid overload.

13 out of 18 severe dengue patients, who survived received 10 ml/kg/hr for 1- 2 hours followed by 7 ml/kg/hr for 2 to 4 hours, 5ml/kg/hr for 6 to 12 hours and after 9 – 18 hours they were on 3ml/kg/hr for 20 - 34 hours. None of these patients received bolus of crystalloid or colloids and total fluid received was within the quantity recommended by Srilankan guidelines. After 5 –6 hours of admission they were also started on ORS in addition to 5 ml/kg/hr of intravenous fluid. These children had clinical fluid accumulation like asictis and pleural effusion. But none of thesechildren developed fluid overload or ARDS and all of them recovered after 30 – 50 hours of fluid therapy.

2 out of 5 children with severe dengue who died had compensated shock with bleeding tendency on admission. One was treated with 2 boluses of 20 ml/kg for ½ - 1 hour, 10 ml/kg/hr for 3 hours, 7 ml/kg/hr for 6 hours andcolloidal transfusion of 10 ml/kg 2 boluses were given over 1 hour. He progressed torefractory shock and expired after 11 hours of admission. Another child received 10ml/kg/hr for 3 hours, platelet transfusion of 10 ml/kg over 15 minutes, colloid transfusion of 10 ml/kg over 1 hour and 7 ml/ kg/hr for 6 hours. He expired 11 hours after admission due to profound shock and ARDS.

The other 3 who died were admitted with bleeding andprofound shock. They were given 2 boluses crystalloids of 20 ml/kg over ½ - 1 hour followed by 10 ml/kg/hr for 5 hours and colloid transfusion of 10 ml/kg over 1 hour.For severe thrombocytopenia they also received platelets. Inspite of this, shock did not improve. They developed ARDS and were managed with ventilator. These children had clinical fluid accumulation like asictis, pleural effusion and expired within 7 hours of admission.

All the 5 deaths occurred within 9 to 11 hours after admission and all died of refractory shock and ARDS and were assisted with ventilator and inotropes. Shock could not be managed with fluid bolus or colloids and high fluid rate of 10ml/kg/hr. This fluid requirement was more than recommended by Srilankan guidelines (fluid rate >150 ml/kg/24 hrs). Whether these high fluid volume contributed to death needs further evaluation through casecontrol studies.

33.3% and 38.9 % patients in severe dengue required platelet and colloidal transfusion respectively, whereas 100 % of patients with dengue with warning signs were treated successfully with isotonic crystalloid solutions, which was similar to the study done by Hung (2012). Platelets were transfused for severe thrombocytopenia. Colloid was transfused for profound shock which could not be managed with higher fluid rates of isotonic fluids. Since there was no gross fall in hematocrit, none of the patient in the present study received blood transfusion.

In the present study, patients who developed severe dengue required a higher volume of fluids from on 5th to 7th day of the illness when compared with dengue with warning signs group which is similar to the study done by Kularatne *et al.*, (2015).

Complications like asictis (31%), pleural effusion (24%) and acute respiratory distress syndrome (5%) were noted and were common in severe dengue,which could have been the cause for mortality in severe dengue patients in our study. Mishra *et al.,* (2016) and Malavige *et al.,* (2006) also had similar findings.

Soller *et al.,* (2016) suggest that optimal fluid management in dengue cases with plasma leakage requires close monitoring, experienced staff, laboratory support and restoration of intravascular volume with avoidance of volume overload, based on the clinical parameters.

Early recognition of illness, careful monitoring and appropriate fluid therapy alone has improved the outcome in 95 % of our study patients. Common cause of death was severe refractory shock and ARDS manifesting singly or in combination. The study done by Singhi *et al.,* (2007) says fluid therapy alone has decreased the mortality to 1%.

Mortality rates in the study by Rangaswamaiah *et al.,* (2017), Narayanan M. et al.(2002), Dhooria *et al.,* (2008), Aggarwal Anju *et al.,* (1998) was 0.53%, 0.8%, 3.7% and 6% respectively with all cases belonging to severe dengue group. In present study, mortality rate of 5 % was observed and mortality was associated with admission 12 – 24 hours after developing critical phase. These cases also received higher

volume of fluid and had fluid overload. Majority of severe dengue patient in the present study were admitted in later part of critical phase and required more fluid. Thus when admitted after 12 to 24 hours of critical period, when plasma leakage is at its height,complications were more common, fluid requirement was much higher than recommended which might have contributed to mortality.

Conclusion

Majority of children in dengue fever are treated successfully with isotonic crystalloid fluids and ORS as recommended by National guidelines of denguemanagement 2014.Severe dengue patients required higher intravenous fluid rates compared topatients with dengue with warning signs. Quantity of fluid received by patients of dengue with warning signs and severe dengue who recovered, was not more than that recommended by Srilankan guidelines. Quantity of fluid administered during critical phase to patients with severe dengue who expired was more than what the Srilankan guidelines had suggested. Complications of fluid overload were seen only in patients who expired withsevere dengue.Colloids and platelet transfusion had less advantage in reducing the mortality in severe dengue.Mortality was higher in severe dengue and was related to profound shock, ARDS and fluid overload.

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