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Original Article

A comparison of outcomes of management of Dengue Haemorrhagic Fever using minimal intervention and the standard management protocol in paediatric units of a Sri Lankan tertiary care facility; A retrospective comparative cross-sectional study

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Abstract

Dengue is a mosquito-borne viral infection found in tropical and sub-tropical climates worldwide. Dengue Fever is a significant health concern in Sri Lanka. Dengue Hemorrhagic Fever is managed following a standard protocol laid down by the Ministry of Health Sri Lanka. During the recent epidemic of dengue a deviation from standard protocol was observed with minimal intervention (i.e. without intravenous fluids and urinary catheterisation).

This study aimed to compare minimal intervention vs. standard protocol with regard to the development of complications and outcomes of children with Dengue Haemorrhagic Fever.

A comparative cross-sectional study was conducted retrospectively using secondary data

The clinical records of paediatric patients with Dengue Haemorrhagic Fever (n=151) admitted to Teaching Hospital, Karapitiya, Galle, Sri Lanka during 2019. The study subjects were categorised into two groups as standard protocol and minimal intervention based on the type of management received.

Of 151 patients , 98 (65%) were managed following standard protocol and 53 (35%) following minimal intervention. No significant differences were observed in the two groups in age (p=0.57), sex (p=0.72), day of fever on admission (p=0.65), and haematological parameters on admission (p>0.05). There was no difference in the recovery and duration of hospital stay in the two groups. However, infections (p=0.04) and fluid overload (p=0.004) were significantly more common in the standard protocol group compared to the minimal intervention group.

Minimal intervention reduces complications of the management of DHF and reduces the burden to the health care system and patients.

Keywords

complications, critical phase, Dengue Hemorrhagic Fever, Fluid overload, Sri Lanka

Introduction

Dengue is a mosquito-borne viral infection found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas (1). The number of dengue cases reported to World Health Organization increased over eightfold over the last two decades, from 505,430 cases in 2000 to over 2.4 million in 2010 and 5.2 million in 2019 (1). Dengue infection has become a significant public health concern in Sri Lanka too (2).

Dengue has a broad spectrum of clinical presentations (3). Dengue haemorrhagic fever is characterised by transient increased vascular permeability leading to plasma leakage. The period during which the fluid is leaked is called the critical phase, which is very dynamic, and the progression of leaking is highly variable from patient to patient (4).Therefore, all suspected patients with DF should be closely followed up to identify whether they develop DHF to carry out meticulous fluid management during the critical phase.

Management of dengue is based on National Guidelines (4). According to the guidelines intravenous (IV) fluids should be started in all the patients who are entering into critical phase. Those who can drink , IV fluids as 0.5ml/kg/hour are given to 'keep vein open' during the critical phase while the balance is given orally. Hourly urine output is the best guide to decide the rate of IV fluid infusion to maintain circulation. Therefore, all high-risk patients such as infants, obese patients, patients with underlying diseases, patients with complications such as shock and platelets below 50,000/mm^3 should be catheterised according to the guidelines. Hematocrit (HCT) measurements of 4-6 hours are indicated in non-shock patients, and it is done more frequently in patients who develop shock.

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During the recent dengue epidemic in 2019, some deviations from guidelines of the management of DHF were observed due to various reasons such as less human resources in the ward, needle phobia and not giving consent for interventions due to cultural issues. These deviations include administrating total oral fluids instead of IV fluids, measurement of urine output without catheterisation, and HCT measurement 12 hourly with full blood counts instead of 4 hourly HCT in patients who showed leaking. This management is named as Minimal Interventions (MI). These deviations from the guidelines have not made much difference in the outcomes according to the experience of clinicians.

This study aimed to compare the outcome of patients managed with different protocol (minimal intervention) with the standard protocol (according to national guidelines) in managing DHF in terms of complications and the patient's overall outcome.

Management of DHF with minimal interventions has already been practiced in some countries. A study conducted in Taiwan with 49 patients with DHF without shock has revealed advantages of oral hydration over intravenous fluid, and patients treated with IV fluids were more prone to develop pleural effusion and pulmonary oedema (9,5). Moreover, Dengue management needs more human resources and laboratory facilities compared to any other vector born disease (11,6). Therefore, it is worth compare outcomes of minimal intervention with standard management protocol in managing DHF. The findings of this research will be helpful to plan a prospective case-control study to compare the outcome of minimal intervention Vs. Standard protocol. Hereby the complications associated with management of DHF can be reduced, and the data will help to revise the guideline of management of DHF.

Methods

A comparative cross-sectional study was carried out retrospectively using secondary data available in the clinical records of paediatric patients with DHF admitted to Teaching Hospital, Karapitiya, during the year 2019. Teaching Hospital, Karapitiya is the only tertiary care facility in the Southern province that caters to paediatric patients and has three general paediatric wards. Paediatric DHF patients from all three wards, who had been diagnosed by hematological parameters and evidence of fluid leakage into the body cavity confirmed by two ultrasound scans, were included in the study. DHF patients who had incomplete DHF monitoring charts were excluded from this study.

The study subjects were categorised into two groups based on the type of management received. Those children who were managed according to the National guidelines for management of DF, i.e. intravenous fluids, urinary catheterisation, and four hourly capillary hematocrit measurements, were categorised as Standard Protocol (SP) group. Patients who received only oral fluids, who were not catheterised and had not, had regular micro hematocrit measurements categorised as Minimal Intervention (MI) group.

The study variables included basic demographic characteristics of the patients, day of fever, hematological/ biochemical parameters, details of fluid management, complications developed during management and the outcomes of management. Relevant data were extracted from the Bed Head Tickets (BHT) and dengue monitoring charts on the BHT using a data extraction sheet. Data analysis was done using SPSS statistical software (Version 20.0). The study subjects who were managed with minimal intervention initially and later changed to SP were excluded from the subsequent analysis.

Statistical significance was analysed by using the Mann-Whitney U test for quantitative data and the Fisher's exact test / Chi-square test for qualitative data. The level of significance was set at 0.05.

The ethical clearance for the study was obtained.(Reference No:- 2020 P 107). Permission for data collection was obtained from the Director, Teaching Hospital, Karapitiya and the Consultant Paediatricians in charge of the paediatric units.

Results

The study sample consisted of 151 DHF patients. Of these patients, 98 (64.9%) had been managed according to the standard protocol (SP), while 53 patients (35.1%) were managed with minimal intervention (MI) at the commencement of treatment. Subsequently, 28 out of these 53 patients (18.5% of the original sample) were excluded from the study due to interventions introduced later during the management such as starting intravenous fluids (n=22) and urinary catheterisation (n=6). Therefore, at the end of the critical phase, the standard protocol group consisted of 98 patients (79.7%), while 25 patients (20.3%) were in the minimal intervention group.

The patients in MI group and SP group were compared with respect to their socio-demographic characteristics, duration of fever on admission and hematological parameters at baseline to ensure that the two groups were comparable. The MI group consisted of 11 males (44%) and 14 females (56%) and the corresponding numbers in SP group were 47 (48%) and 51 (52%). Fisher's exact test indicated that there were no significant gender differences between the two groups (p=0.723). Similarly, no statistically significant differences were noted in age, day of fever and the haematological/

biochemical parameters at baseline between the two groups as shown in Table 1.

Table 1. Comparison of the age, duration of fever and haematological parameters on admission between two study groups

Variable	Standard protocol (N=98)		Minimal intervention (N=25)		p value*
	Median	Interquartile range	Median	Interquartile range	
Age in months	111	84	120	80.5	p = 0.579
Day of fever on admission	4	1	4	2	p= 0.657
Total while cell count (mm^3/L)	4.38	2.62	4.53	3	p= 0.499
Hematocrit	39	6.42	38	4.7	p= 0.905
=Platelet count (mm^3/L)	88	77.25	108	54	p= 0.453

**Mann–Whitney U test*

The lowest platelet count, highest recorded haematocrit and the highest recorded levels of liver enzymes were compared between the SP group and MI group during the critical phase. There was no significant difference in the lowest platelet count during the critical phase in two groups (p=0.772), however, a statistically significant difference was observed in the highest AST (p=0.004) / ALT (p=0.044) and the highest recorded haematocrit (p=0.009) in two groups, all three parameters being higher in the SP group (Table 2).

Table 2. Comparison of selected hematological and biochemical parameters during the critical phase between the two study groups

Variable	Standard protocol (N=98)		Minimal intervention (N=25)		p value*
	Median	Interquartile range	Median	Interquartile range	
Lowest Platelet Count (mm^3/L)	31	22.5	33	24	p= 0.772
Highest AST (IU/L)	127	107	73	91	p= 0.004
Highest ALT (IU/L)	52	55	34	79.25	p= 0.044
Highest recorded Hematocrit	43	5	41	4.6	p= 0.009

**Mann–Whitney U test*

Approximately 50% (n=62) of the patients in the sample developed complications of management of whom 61 belonged to the SP group. The proportions with complications were compared between the two study groups and the results are presented in the Table 3**.**

Table 3. Comparison of the complications between two study groups

Complications	Standard protocol (N=98)		Minimal intervention (N=25)		p value
	Number	%	Number	%	
Secondary Infections					
Yes	16	16.3	0	0.0	p=0.040*
No	82	83.6	25	100.0	
Bilateral Pleural effusion					
Yes	32	32.7	1	4.0	p=0.004**
No	66	67.3	24	96.0	
Fluid overload with dyspnea					
Yes	25	25.5	0	0.0	p=0.005**
No	73	74.5	25	100.0	

Fisher's exact test *** Chi-square test*

When considering fluid overload, bilateral pleural effusion was present in one patient (4%) in the MI group compared to 32 patients (32.7%) in the SP group and this difference was statistically significant (p=0.004). Dyspnoea due to fluid overload was detected in 25 patients (25.5%) in the SP group, and none had developed dyspnoea due to fluid overload in the MI group (p=0.005). Ascites was detected in three patients (3.1%), and generalised oedema was seen in five patients (5.1%) in the SP group and none had developed ascites or generalised oedema in the MI group, however, this difference was not statistically significant (p>0.05). In managing fluid overload, nearly 14% of the patients in the SP group required intravenous furosemide compared to none in the MI group.

Secondary infections were another complication observed in the SP group (n=16, 16.3%) but the patients of the MI group have not had any secondary infections during the illness, the difference being statistically significant (p=0.04). Cannula site infection (6%), septicemia (6%) and UTI (4%) were the types of infections observed.

Fluid quota is a guide for fluid therapy during the critical phase of DHF. It is calculated by adding 5% extra fluid to the maintenance therapy for 24 hrs. In our study sample, the minimal intervention group only needed 80% of the fluid quota, whereas the standard protocol group needed 91% of the fluid quota. This difference of the percentage of fluid quota used in the two groups was statistically significant (p<0.0001; Fisher's exact test).

All the patients in our study sample recovered with or without complications (Table 4). Five out of 123 patients (5.3%) have been admitted to the Intensive Care Unit (ICU) due to shock on admission (n=1), bleeding (n=2) fluid overload (n=2), and septicemia (n=1), whereas none (0%) needed ICU care in the minimal intervention group (p<0.001). The median duration of hospital stay in patients managed according to standard protocol or with minimum intervention was 5 days (interquartile range: 2 days and 2 days, respectively).

Table 4. Comparison of the final outcome of the patients in two study groups

Outcome	Standard protocol (N=98)		Minimal intervention (N=25)		p value*
	Number	%	Number	%	
Fatalities					
Yes	0	0.0	0	0.0	-
No	98	100.0	25	100.0	
Needed ICU care					
Yes	5	5.3	0	0.0	p<0.001
No	93	94.7	25	100.0	
Recovered					
With complications	61	62.2	1	4.0	p<0.001
Without complications	37	37.8	24	96.0	

*Chi-square test

When comparing the development of complications, 61 (62%) patients in the SP group had developed at least one complication compared to only one patient (4%) in the MI group and this difference was statistically highly significant (p<0.0001).

Discussion

This study attempted to compare the development of complications and the final outcome of pediatric dengue patients managed according to standard management protocol or with minimal intervention in a tertiary care facility in 2019. The analysis was based on secondary data extracted from the clinical records of these patients. The findings revealed that the minimal intervention approach is equally effective in managing patients while minimising the risk of complications due to management.

There is no specific therapy for Dengue Fever. Meticulous fluid management is the mainstay of treatment in DF that is currently governed by consensus guidelines rather than by strong research evidence (7). Therefore, scientific evidence in favour of adopting a minimal intervention approach in uncomplicated dengue patients may lessen the burden of the health care system in the face of an increasing number of cases.

Sri Lanka has reached the lowest-ever dengue case fatality rate of <0.2% in 2018 (8). In keeping with this trend, there were no fatalities in our sample. However, complications such as fluid overload and infections were high among the standard protocol group (p<0.0001). Fluid overload seems directly related to intravenous fluid therapy. The percentage of fluid quota given during the critical phase is significantly high in the SP group who received intravenous fluids compared to the MI group who had only oral fluids. Two children needed ICU care due to fluid overload. The WHO and national guidelines emphasise the crucial importance of restrictive fluid resuscitation to minimise fluid overload (3,4). Therefore, we suggest that oral rehydration therapy would be a better option in children with uncomplicated DHF, minimising the risk of fluid overload.

All the patients in our study group have survived, and it was found that patients who received intravenous fluid were prone to develop pleural effusion and/or pulmonary oedema. There are not many studies found to compare the results of our study. A study conducted in Taiwan in 2007 has revealed the advantages of oral hydration over intravenous fluid in adult patients and concluded that oral hydration might be as effective as intravenous fluid replacement for adults with non-shock DHF (9,5). However, the fluid requirement of children is different from adults, and the conclusion for this study has to be interpreted cautiously. Another limitation of this study is that it has not mentioned the type of oral fluid used, whereas in the present study, Oral rehydration fluid was used as the main therapy.

The other main complication found in our study population is sepsis, which was also seen only in the SP group (p<0.004). Urinary tract, cannula site infections, and septicaemia were the causes.

Dengue management needs more human resources and laboratory facilities compared to any other vector-borne disease (10,6). Frequent HCT measurements need a lot of workforces and are time-consuming, especially during epidemics. None of the patients in the MI group had regular HCT measurements in our study population, which indicates four-hourly HCT measurements are not mandatory in the management of every DHF patient. However, further prospective studies are needed to determine the frequency of HCT measurements in DHF.

To our knowledge, this study is the first attempt at analysing the outcomes of two different management options for DHF in paediatric patients. The findings of this study will be important for clinical decision-making and the formulation of national guidelines in the future.

This study was conducted using data extracted from the clinical records of patients with dengue fever managed at a tertiary care facility over one year. Although a clinical trial would have been the ideal design for a study of this nature, one advantage of using secondary data is that the likelihood of information bias due to differential reporting or differential care given to the patients was minimal as the data has already been recorded. Further, the ethical issues in assigning the intervention do not arise in using secondary data.

The present study is limited by its small sample size, which could explain the failure to detect statistically significant differences in some parameters compared. Further, as this is a retrospective study, patients' clinical parameters, which give a clearer picture of the patients, were not analysed in-depth, and the study was a single-centre experience. Nevertheless, in the absence of scientific evidence on the effectiveness of the current management protocol, we believe that this study will serve as a first step towards planning well-designed clinical trials to compare minimal intervention approach and standard protocol in the management of DHF in the future.

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