



Study of Low Dose Diuretic Infusion: A Double Edged Weapon Used in the Management of Dengue Fever with Warning Signs.

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I. INTRODUCTION

Dengue is the most common mosquito-borne viral illness worldwide. The global incidence has increased in recent decades. Every year, hundreds of thousands of severe cases arise, of which 20,000 lead to death¹. The virus responsible for causing dengue, is called dengue virus. There are four Dengue virus serotypes, meaning that it is possible to be infected four times².

Dengue virus is transmitted by female mosquitoes mainly of the species **Aedes aegypti** and, to a lesser extent, **Ae. albopictus**. These mosquitoes are also vectors of chikungunya, yellow fever and Zika viruses. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature, relative humidity and unplanned rapid urbanization³.

Dengue is a severe, flu-like illness that affects infants, young children and adults, but seldom causes death. Symptoms usually last for 2–7 days, after an incubation period of 4–10 days after the bite from an infected mosquito⁴.

The World Health Organization classifies dengue into 2 major categories: dengue (with / without warning signs) and severe dengue. The sub-classification of dengue with or without warning signs is designed to help health practitioners triage patients for hospital admission, ensuring close observation, and to minimise the risk of developing the more severe dengue⁴.

Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of the following symptoms during the febrile phase includes severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands rash⁴.

A dengue patient enters what is called the critical phase normally about 3-7 days after illness onset. It is at this time, when the fever is dropping (below 38°C/100°F) in the patient, that warning

signs associated with severe dengue can manifest. Severe dengue is a potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment⁴.

Warning signs should be identified as early as possible which include severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness, blood in vomit. If patients manifest these symptoms during the critical phase, close observation for the next 24–48 hours is essential so that proper medical care can be provided, to avoid complications and risk of death⁴.

Furosemide (LASIX) is a diuretic which acts on a distal tubule by inhibiting carbonic anhydrase and it also abolishes corticomedullary osmotic gradient and blocks negative and positive free water clearance⁷.

II. AIMS AND OBJECTIVES

To determine appropriate time and safety of Low Dose Inj furosemide infusion in children with dengue fever with warning signs to prevent progression to ARDS.

III. MATERIALS AND METHODS

The study was a cross sectional study conducted in Shamanur Shivashankarappa Institute of Medical Sciences, Davangere from December 2018 to June 2019.

- 20 children who presented with dengue fever with NS1 positive/ IgM positive were admitted to wards and was treated according to latest WHO guidelines with 0.9% normal saline (3ml/kg/hr) and vitals was monitored.
- On appearance of warning signs especially mild respiratory distress, abdominal distension, severe abdominal pain, persistent vomiting with no hemodynamic instability patients were selected. The patients were regularly monitored for their



abdominal girth with their pulse rate, respiratory rate, urine output, blood pressure.

• Low dose Inj furosemide infusion (0.05mg/kg/hr) was started in patients who complained of abdominal pain with mild tense abdomen and was continued and monitored very closely and infusions were given 24 to 48 hrs.

Out of 20 children in our study, 17 patients showed early signs of recovery in terms of decreased abdominal distension, decreased respiratory distress and improvement in platelet count.

• 3 patients progressed to hypovolemia. It was difficult to assess if hypotension was due to diuretic or progression of the disease per se.

• No deaths were seen in the study.

IV. RESULTS

In this study conducted, 13 patients were male (65%) and 7 patients were female (35%).

SEX	No. of Patients	Percent
Male	13	65.0
Female	7	35.0
Total	20	100.0

Table no. 1

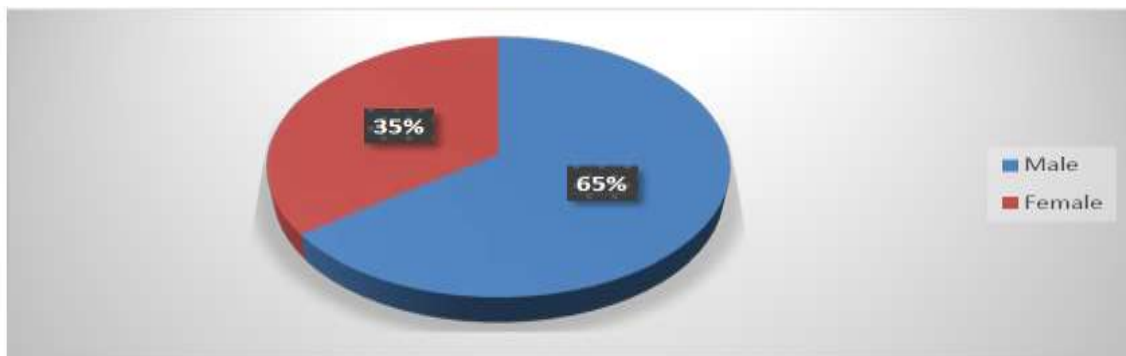
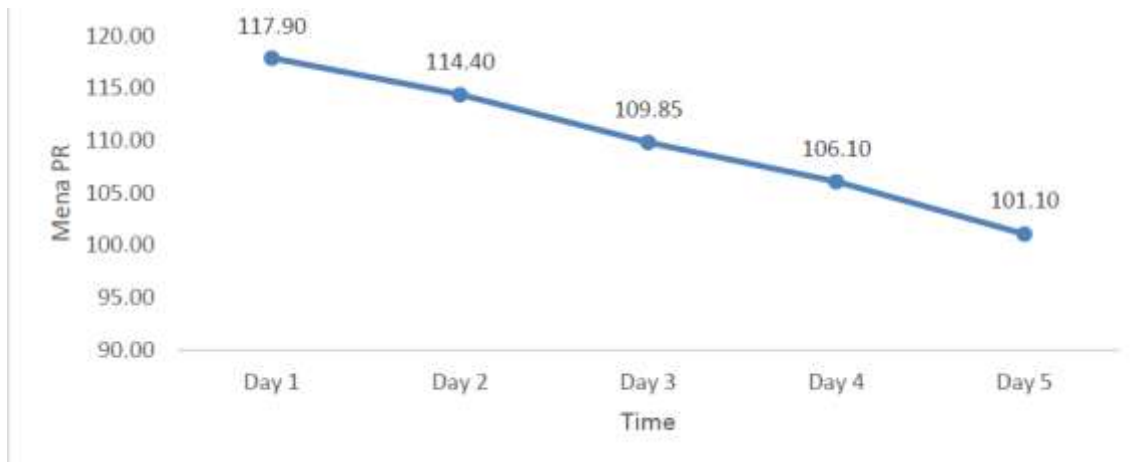


Fig - 1

In our study, pulse rate pattern showed tachycardia initially during the stage of warning signs was found to reduce as the infusion of Inj LASIX was started and was statistically significant as Shown in TABLE 2 and graph 1.

PR	Mean	Std. Deviation	p value
Day 1	117.90	15.808	0.000
Day 2	114.40	19.880	
Day 3	109.85	17.983	
Day 4	106.10	15.430	
Day 5	101.10	10.310	

Table 2: Study of relation of pulse rate with respect to lasix infusion.

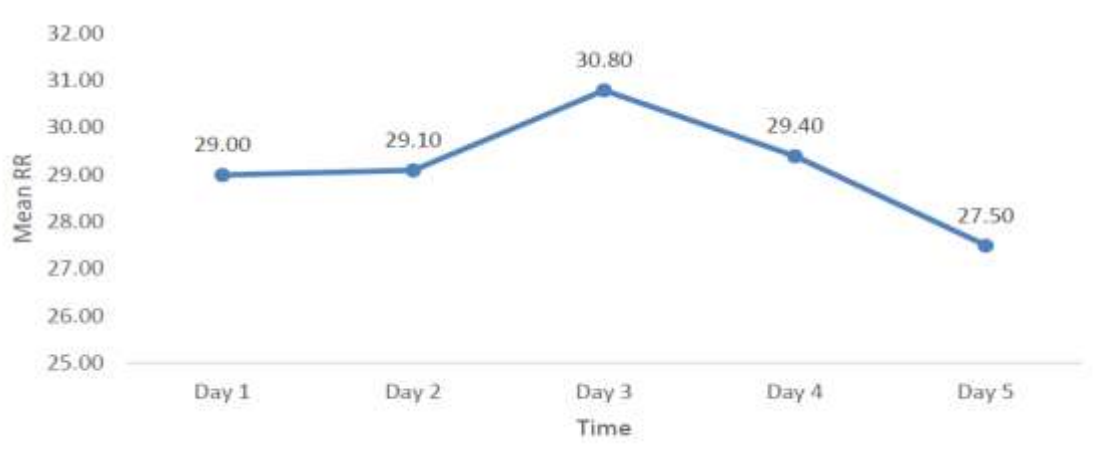


Graph : 1 Study of relation of pulse rate with respect to lasix infusion.

- In our study the respiratory rate pattern showed slight tachypnoea as the abdominal distension increased during the initial stage of the disease and gradually reduced on starting with Inj LASIX infusion as shown in Table 3 and Graph 2.

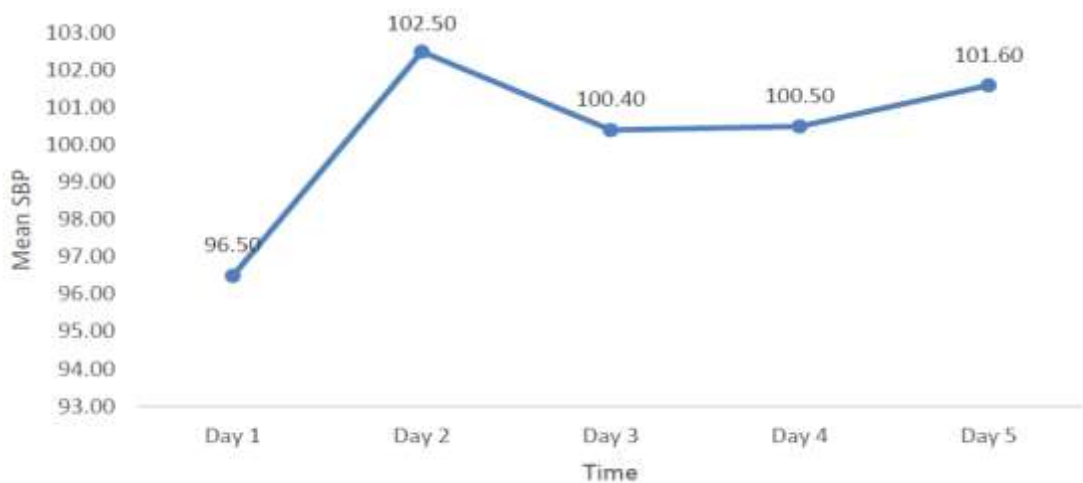
RR	Mean	Std. Deviation	p value
Day 1	29.00	4.129	0.006
Day 2	29.10	4.025	
Day 3	30.80	5.327	
Day 4	29.40	4.903	
Day 5	27.50	4.583	

Table : 3 Study of relation of respiratory rate with respect to lasix infusion.

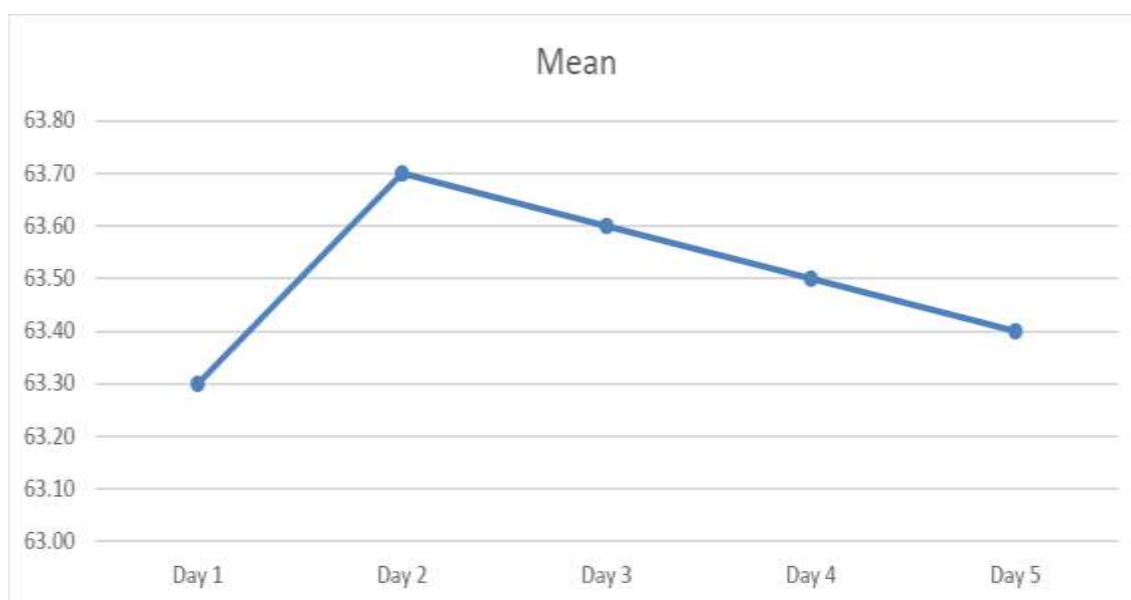


Graph :2 Study of relation of respiratory rate with respect to lasix infusion.

- The blood pressure pattern showed slight decrease in systolic blood pressure on starting the Inj LASIX infusion but was more than the 5th centile, similarly diastolic blood pressure was also slightly decreased, but was more than 5th centile, only 3 patients among the 20 developed hypotension with SBP and DBP between 5th and 10th centile.



Graph :3 Study of mean systolic blood pressure in relation to lasix infusion.



Graph :4 Study of mean diastolic blood pressure in relation to lasix infusion.

- In our study the platelet count pattern showed a drastic drop in platelet count in all patients before starting of low dose Inj LASIX infusion and it showed to slightly increase as the Inj LASIX infusion was started and it is depicted below in the table.

Platelet Count	Mean	Std. Deviation	p value
Day 1	88850.00	45572.701	0.019
Day 2	59750.00	26759.897	
Day 3	54550.00	26434.577	
Day 4	71000.00	47538.350	
Day 5	93400.00	63936.152	

Table : 4 study of platelet count in relation to lasix infusion.

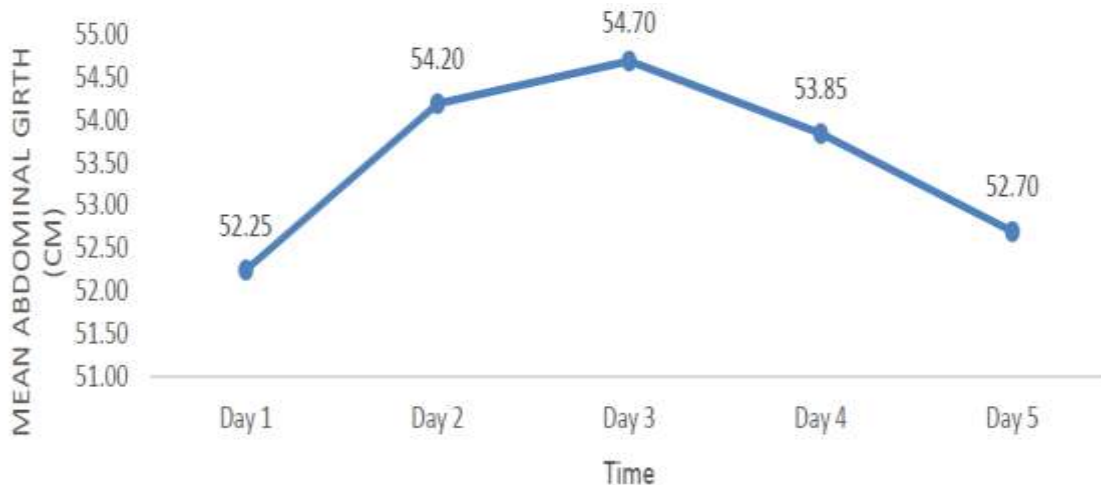


Graph : 5 Study of platelet count in relation to lasix infusion.

- In our study, the abdominal girth pattern showed increasing trend initially as the patient started to get warning signs. Later the abdominal girth slowly started to reduce as the Inj LASIX infusion was started.

ABDOMINAL GIRTH (CM)	Mean	Std. Deviation	p value
Day 1	52.25	8.990	0.000
Day 2	54.20	9.317	
Day 3	54.70	8.957	
Day 4	53.85	8.845	
Day 5	52.70	8.767	

Table : 5 Study of abdominal girth in relation to lasix indusion.



Graph : 6 Study of abdominal girth in relation to lasix infusion.



VI. DISCUSSION:

- This study demonstrated the efficacy of low dose furosemide infusion in dengue fever with warning signs to prevent the patients from progressing to ARDS by using it in early stages of dengue.

A study conducted by **reddy, et al.** a prospective study conducted at Indira Gandhi Institute of Child Health, Bangalore.

There was a significant difference in survival between those children who received low dose furosemide infusion alone and those who failed diuretic therapy and required mechanical ventilation.

Significant increase in all parameters of arterial blood gases was noted following low dose furosemide infusion, thus demonstrating an improvement in oxygenation.

This study also says that, low dose Furosemide infusion improves survival in the management of Dengue fever with ARDS, with significant improvement in oxygenation **But, this study did not mention about the time of infusion of inj lasix.**

Another article namely **Clinical Manifestations and Management of Dengue/DHF/DSS by Siripen Kalayanarooj.** quoted that the most common complication in DHF/DSS management is fluid overload, which may lead to heart failure, acute pulmonary edema or even death if not managed properly with adequate time..

Early detection of signs and symptoms of fluid overload includes puffy eyelids, tachypnoea, distended abdomen with abdominal discomfort.

Late signs of fluid overload includes Cough, respiratory distress, very tense abdomen, impending respiratory failure.

So, we conducted our study to know whether by using diuretic by low dose furosemide infusion in early stages of dengue fever would be beneficial in preventing progression of disease to ARDS.

A study by name **CAPILLARY LEAK SYNDROME IN SEVERE DENGUE-** by **Tapan Biswas** quoted that, in Dengue, there was massive platelet destruction & also destruction of RBC, WBC, from these cell huge amount of cytokine are released. In severe dengue huge number of platelet destruction and released enormous amount of cytokines, activate the complement system which increased vascular permeability and ultimately lead to capillary leak syndrome.

Due to molecular mimicry between dengue virus and platelet; more platelet are destructed than others cells.

In Our study, there was improvement in almost 17 patients who were started on low dose Inj LASIX infusion with no hemodynamic instability.

3 patients had features of hypovolemia and hypotension, so low dose Inj LASIX infusion was stopped in these patients and was treated with regular WHO dengue guidelines until the patient vitals improved and meticulous monitoring was done for these patients.

- None of the patient succumb to death in our study.
- The only limitation of this study is minimal sample size, that was because parameters took for this study did not satisfy to include many patients in the study, but we would like to further continue this study and prepare some set parameters and minimal criteria's to satisfy before starting low dose Inj LASIX infusion in patients of dengue fever with warning signs and no hemodynamic instability to prevent progression to ARDS.

VII. CONCLUSION :

- This study was done to know the beneficial effects of low dose inj furosemide infusion in dengue fever patients with warning signs in paediatric wards to halt the further worsening of dengue fever to ARDS and stop impending failure.
- The study helps to avoid intensive care unit admission by regular monitoring of enclosed parameters in wards by early introduction of Inj LASIX in paediatric wards. So cases early warning signs of dengue can be identified as soon as possible and well managed in wards only with continuous monitoring of the patient.
- So, by using low dose Inj LASIX infusion in early stages of dengue fever with warning signs, we could prevent the patients progression to ARDS with regular monitoring of vitals.
- Low dose injection lasix infusion act as double edge weapon, initial stages with early identification of warning signs can well managed by this drug as we seen in this study, but certain stages of disease course of illness, this drug will act as double edge sword and patient deteriorates and lead to threatening complications.

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