RESEARCH
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EFFECT OF NUTRITIONAL STATUS ON OUTCOME OF DENGUE INFECTION IN CHILDREN

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Abstract

Introduction: The anthropometric measurements are commonly used for nutritional assessment in children to classify nutritional status into four categories: normal, wasting, stunting and overweight. However, children can experience concurrent stunting and wasting. Similarly, they can also experience stunting and overweight. These conditions are associated with greater susceptibility to mortality and chronic diseases, and they are now seen as a specific problem requiring special attention. In patients with severe dengue infection, early diagnosis and proper supportive care can reduce the risk of mortality. Identifying risk factors associated with severe forms of dengue infection is crucial to accurately select patients most likely to benefit from appropriate early interventions. Previous studies have explored the impact of malnutrition, defined as a disorder of nutritional status, including undernutrition (wasting, stunting and underweight) and overnutrition (overweight and obesity) on dengue severity, but findings have been inconsistent. Hence, the present study was carried out to assess the effect of nutritional status on outcome of dengue infection in children. **Methodology:** This was a descriptive Cross-Sectional Study carried out over a period of 2 years from October 2020 to September 2022 amongst children of age between 1 year to 16 years admitted in the department of Paediatrics at Saveetha Medical College and Hospital, Thandalam with symptoms of fever, abdominal pain, vomiting and /or reduced urine output. Dengue infection was diagnosed based on clinical signs and symptoms with positive NS1antigen if they present within 5 days or IgM/IgG if they present after 5 days of illness. Anthropometric measurements were done and the children were classified as stunted/normal based on height, underweight/normal based on weight and obese, normal or malnourished based on BMI. Severity of illness was assessed based on days of hospital stay, PICU admission, shock. Standard statistical methods were used to determine the correlation between nutritional status and severity of dengue infection. Qualitative data was analysed by Chi Square test which express the frequency and percentage of the data. Quantitative data was expressed as Mean and standard deviation which was analysed by student independent t test. A p value lower than 0.05 was considered as statistically significant. **Results:** The mean age of children in the present study was 8.9 years. Underweight children were found only in Low and Middle SES group and the percentage was 9% and 11% respectively. The percentage of children with obesity was more in the middle and upper SES 22.22% and 14.2% respectively. NS 1 Antigen was positive in 53.8%, Dengue IgM positivity rate was 84.6% and Dengue IgG was positive in 26.1% of the study population. Subjects who were stunted had more prevalence of shock and PICU admission as compared to subjects with normal height.9.2% children in the study population were underweight. PICU admission had no statistical significance with weight for age. Days of stay in hospital was found to be more in obese and normal weight children. 25% of children with under nutrition had PICU admission and 50% of children with under nutrition developed shock. **Conclusion:** Although undernourished children are more likely to suffer from severe dengue, there was no significant correlation between nutritional status of child with the severity of dengue infection.

Keywords: Dengue Infection, Nutrition, Malnourishment.

INTRODUCTION

Studies examining the severity of dengue and nutritional status have resulted in controversial outcomes. Nutrition is considered an important determinant of immune function. Previous studies have suggested that in either primary or secondary DENV infection, an exacerbated host immune response might play a pivotal role in pathogenesis of severe dengue disease. The effect of under nutrition might be associated with a dysfunction of the innate and adaptive immune systems. For example, lower lean mass deposition has been related to persistent low-level inflammation among Gambian adolescents. Specifically, under-nutrition impairs immune priming by dendritic cells and monocytes and impairs effector memory T-cell function.1 Eleven studies have examined the relation between the severity of dengue disease and nutritional status of child with inconclusive results. 2Some studies found that patients with excessive body weight were at increased risk of severe dengue. Those who were overweight with normal stature were at risk for developing severe dengue infection.

For overweight children with a normal stature, their status suggests that they did not experience substantial difficulties owing to limitations in food access, as their growth occurred within the expected range and being overweight may be a result of a systemic positive energy balance. A growing body of evidence suggests that obesity-associated increase in chronic, low-grade inflammation with excess production of leptin, interleukin-1β, interleukin-6 and tumour necrosis factor-α and reduction in adiponectin (anti-inflammatory) levels affects immune cell function during infection. It is believed that malnutrition is a protective factor due to suppressed immune activation. In contrast, some studies showed no correlation between severity of dengue illness and nutritional status of the child.21

Hence, the present study was carried out to assess the effect of nutritional status on outcome of dengue infection in children.

METHODOLOGY

This was a descriptive Cross-Sectional Study carried out over a period of 2 years from October 2020 to September 2022 amongst children of age between 1 year to 16 years admitted in the department of Paediatrics at Saveetha Medical College and Hospital, Thandalam with symptoms of fever, abdominal pain, vomiting and or reduced urine output. Dengue infection was diagnosed based on clinical signs and symptoms with positive NS1antigen if they present within 5 days or IgM/IgG if they present after 5 days of illness. Children with pre-existing renal, hepatic and cardiac co morbidities; those with malignancies, trauma, burns, post-operative children and those with mixed infections were excluded from the study. Anthropometric measurements were done and the children were classified as stunted/normal based on height, underweight/normal based on weight and obese, normal or malnourished based on BMI. Severity of illness was assessed based on days of hospital stay, PICU admission, shock. Standard statistical methods were used to determine the correlation between nutritional status and severity of dengue infection. Data was entered in MS Excel sheet. Statistics were held with SPSS software (SPSS 20.0 for Windows, IBM Co). Qualitative data was analysed by Chi Square test which express the frequency and percentage of the data. Quantitative data was expressed as Mean and standard

deviation which was analysed by student independent t test. A p value lower than 0.05 was considered as statistically significant.

RESULTS

A total of 65 cases were recruited in the study. The mean age was 8.9 years. The male and female distribution was nearly equal, with 33 boys and 32 girls in the study group. The anthropometric details of the study population are as depicted in Figure 1. The nutritional status of the study group was normal in the majority of the study population. Gender distribution was comparable and there was no statistically significant variation. However, stunting and underweight was more common in girls as compared to boys.

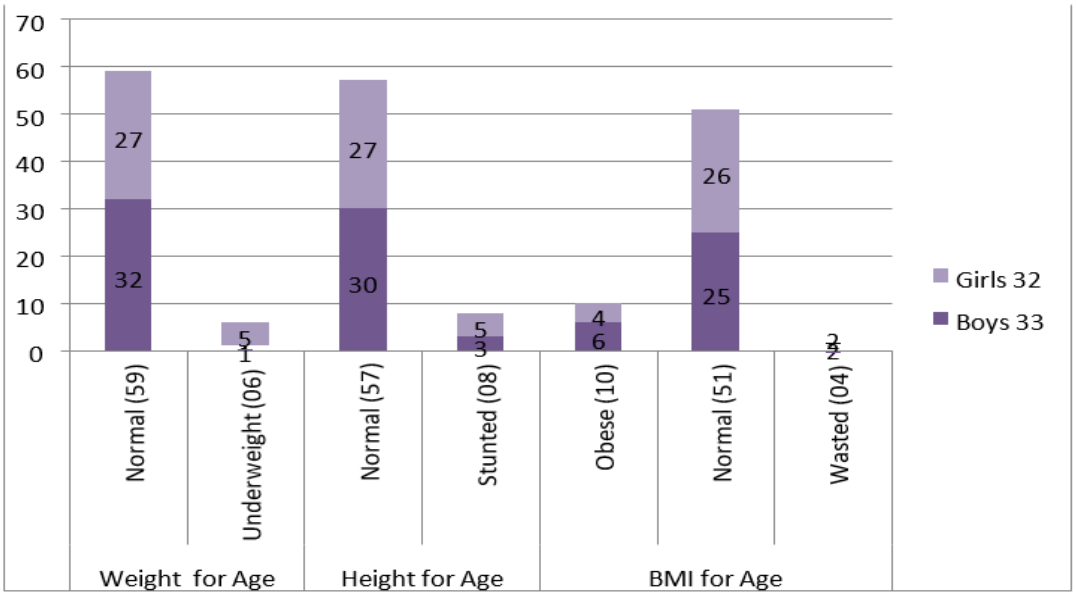

Figure 1: Anthropometry details of study population

The test positivity rates for dengue serology are depicted in Fig 2. NS 1 Antigen was positive in 53.8%, Dengue IgM positivity rate was 84.6% and Dengue IgG was positive in 26.1% of the study population.

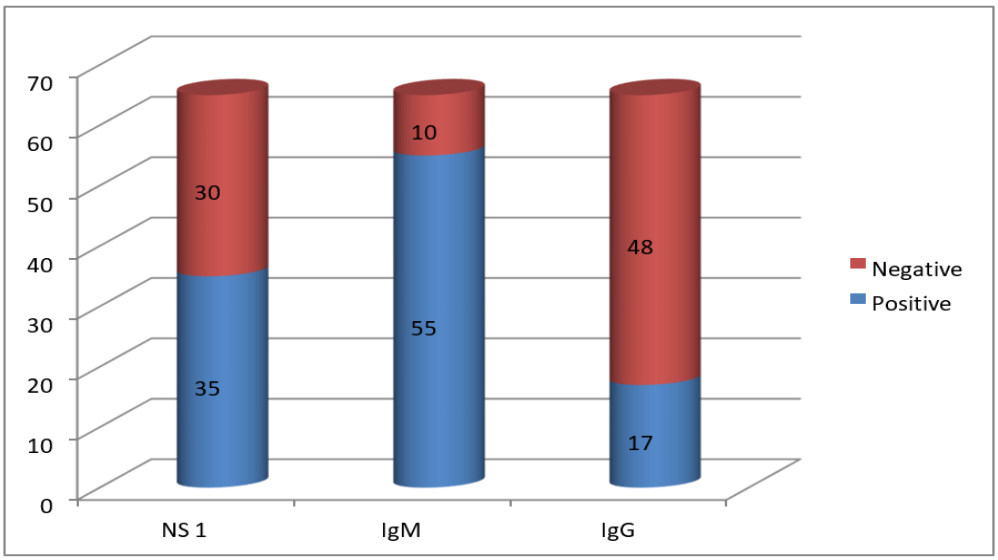

Fig 2: Test positivity

Table 1: Comparison of Stay, Shock and symptoms with the height of child

Factors		Height for Age		□2	p – value
		Normal (57) N (%)	Stunted (08) N(%)		
Days of Stay	3- 5 days	28 (49.1)	03 (37.5)	1.247	0.606
	6-7 days	17 (29.8)	04 (50)		
	8 –10 days	12 (21.1)	01 (12.5)		
PICU	No	48 (84.2)	07 (87.5)	0.058	0.809
	Yes	09 (15.8)	01 (12.5)		
Shock	No	33 (57.9)	03 (37.5)	1.181	0.277
	Yes	24 (42.1)	05 (62.5)		
		SYMPTOMS			
Abdominal Pain	No	26 (45.6)	04 (50)	0.054	0.816
	Yes	31 (54.4)	04 (50)		
Vomiting	No	22 (38.6)	04 (50)	0.38	0.538
	Yes	35 (61.4)	04 (50)		
Fluid Accumulation	No	52 (91.2)	06 (75)	1.923	0.166
	Yes	05 (8.8)	02 (25)		
Mucosal Bleeding	No	52 (91.2)	07 (87.5)	0.116	0.733
	Yes	05 (8.8)	01 (12.5)		
Lethargy	No	45 (78.9)	04 (50)	3.168	0.6
	Yes	12 (21.1)	04 (50)		
Hepatomegaly	No	30 (52.6)	05 (62.5)	0.275	0.6
	Yes	27 (47.5)	03 (37.5)		

***p<0. 1 - *p<0.05 (alpha Value) -PICU – Pediatric Intensive Care Unit.

Table 1 Compares the duration of hospital stay, and circulatory shock among children with Normal and stunted children. Subjects who were stunted had more prevalence of shock and PICU admission as compared to subjects with normal height. Symptoms like abdominal pain, vomiting and hepatomegaly was more pronounced in individuals with normal height. On the other hand, fluid accumulation, mucosal bleeding, lethargy and hepatomegaly were more pronounced in individuals with stunted growth. However stunting had no statistical significance with any of the parameters that were compared.

Table 2: Comparison of Stay, Shock and symptoms with weight of child

Factors		Weight for Age		□2	p – value
		Normal (59) N (%)	Underweight (06) N (%)		
Days of Stay	3-5 days	28 (47.5)	03 (50)	0.328	0.976
	6-7 days	19 (32.2)	02 (33.3)		
	8-10 days	12 (20.3)	01 (16.7)		
PICU	NO	49 (83.1)	06 (100)	1.202	0.273
	Yes	10 (16.9)	0		
Shock	No	33 (55.9)	03 (50)	0.078	0.781
	Yes	26 (44.1)	03 (50)		
		SYMPTOMS			
Abdominal Pain	No	27 (45.8)	03 (50)	0.039	0.843
	Yes	32 (54.2)	03 (50)		
Vomiting	No	23 (39)	03 (50)	0.275	0.6
	Yes	36 (61)	03 (50)		
Fluid Accumulation	No	53 (89.8)	05 (83.3)	0.239	0.625
	Yes	06 (10.2)	01 (16.7)		
Mucosal Bleeding	No	53 (89.8)	06 (100)	0.672	0.412
	Yes	06 (10.2)	0		
Lethargy	No	45 (76.3)	04 (66.7)	0.271	0.603
	Yes	14 (23.7)	04(33.3)		
Hepatomegaly	No	32 (54.2)	03 (50)	0.039	0.843
	Yes	27 (45.8)	03 (50)		

***p<0.01 - *p<0.05 (alpha Value) PICU – Pediatric Intensive Care Unit.

The underweight children in the study population were 9.2% only. Comparison of Stay, Shock and symptoms between normal and underweight showed that being underweight did not have much effect on average stay in hospital and presence of shock. Fluid accumulation, lethargy and hepatomegaly were seen more commonly in underweight individual, though it did not have any statistical significance. On the other hand, abdominal pain, vomiting and mucosal bleeds were more pronounced in children with normal weight. PICU admission had no statistical significance with weight for age, though none of the underweight children required monitoring in PICU. The percentage of children requiring prolonged admission was greater in children with normal weight.

Table 3: Comparison of Stay, Shock and symptoms with BMI for age

Factors		BMI for Age			□2	p –value
		Obese (10) N (%)	Normal (51) N (%)	Wasted (04) N (%)		
Days of Stay	3-5 days	05 (50)	23 (45.1)	03 (75)	2.309	0.706
	6-7 days	02 (20)	18 (35.3)	01 (25)		
	8-10 days	03 (30)	10 (19.6)	0		
PICU	No	09 (90)	43 (84.3)	03 (75)	0.856	0.67
	Yes	01 (10)	08 (15.7)	01 (25)		
Shock	No	06 (60)	28 (54.4)	02 (50)	0.301	0.933
	Yes	04 (40)	23 (45.1)	02 (50)		
SYMPTOMS						
Abdominal Pain	No	04 (40)	23 (45.1)	02 (50)	1.466	0.534
	Yes	06(60)	28 (54.9)	02 (50)		
Vomiting	No	04 (40)	20 (39.2)	02 (50)	0.386	0.916
	Yes	06(60)	36 (60.8)	02 (50)		
Fluid Accumulation	No	09 (90)	45 (88.2)	04 (100)	0.542	0.763
	Yes	01 (10)	06 (11.8)	0		
Mucosal Bleeding	No	09 (90)	47 (92.2)	03 (75)	2.061	0.361
	Yes	01 (10)	04 (07.8)	01 (25)		
Lethargy	No	07 (70)	39 (76.5)	03 (75)	0.528	0.868
	Yes	03 (30)	12 (23.5)	01 (25)		
Hepatomegaly	No	08 (80)	25 (49)	02 (50)	3.273	0.212
	Yes	02 (20)	26 (51)	02 (50)		

***p<0.01 - *p<0.05 (alpha Value) PICU – Pediatric Intensive Care Unit.

Days of stay in hospital was found to be more in obese and normal weight children. There is no statistical difference between PICU stay and presence of shock based on BMI. Fluid accumulation was found to be more in obese children as compared to normal and wasted children. Comparatively most subjects with abdominal pain, vomiting and lethargy were obese. Children with wasting had more mucosal bleeding and hepatomegaly. Around 60% of obese children had abdominal pain and around 30% of them had lethargy.

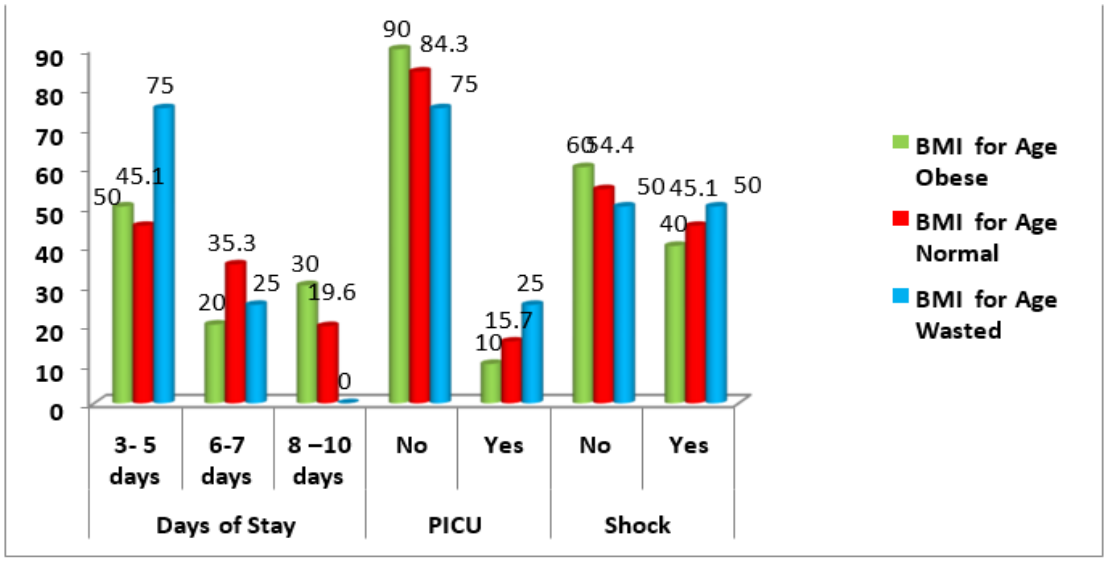

Figure 3: Comparison of Stay, and Shock between Obese, Normal and Wasted (based on BMI for age) in dengue affected children

Figure 3 illustrates the comparison of Stay, and Shock between Obese, Normal and Wasted (based on BMI for age) in dengue affected children. Obese children had more stay around 8-10 days in hospital. 25% of children with wasting had stay in PICU and 50% developed shock too.

Table 6: Comparison of demographic, Blood parameter, Renal and Liver parameter with weight of child

Parameter	Weight for Age		t - value	p- value
	Normal Mean ± SD N = 59	Underweight Mean ± SD N = 06		
DEMOGRAPHIC PROFILE				
Age	9.47 ± 3.505	4.00 ± 1.41	3.772	0.000**
CIRCUMFERENCE				
Mid Upper Arm Circumference	19.55 ± 1.94	13.91 ± 1.15	2.185	0.003***
BLOOD PARAMETER				
Haemoglobin	12.49 ± 1.81	12.15 ± 1.75	0.443	0.659
Platelets	0.975 ± .644	0.985 ± .663	-0.03	0.973
Packed cell	37.84 ± 4.57	39.48 ± 3.51	-0.85	0.391
Total Leucocyte count	4470.73 ± 1862.3	4910.03 ± 2208.66	-0.54	0.51
RENAL PARAMETER				
Urea	19.06 ± 6.57	20.33 ± 20.33	-0.45	0.657
Creatinine	0.491 ± 0.122	0.3500 ± 0.104	2.732	0.008***
LIVER PARAMETER				
SGOT	134.32 ± 123.44	185.50 ± 181.37	-0.93	0.3
SGPT	58.6 ± 58.7	76.83 ± 104.26	-669	-506
ALP	154.40 ± 49.12	136.50 ± 45.73	0.836	0.406

Values are expressed as Mean ± SD; p value calculated using independent student – t test, *p<0.05- ***p<0.01- statistically significant, ns- not significant,

Comparing the anthropometry and laboratory parameters, it was found that children with normal weight were more affected with dengue than children who are underweight. Dengue infection was statistically more common in children with better

nutrition as assessed by MUAC. Among the laboratory parameters only serum creatinine was significantly elevated in normally nourished children as compared to malnourished children.

Table 4: Comparison of demographic, Blood parameter, Renal and Liver parameter with height

Parameter	Height for Age		t - Value	p-value
	Normal Mean ± SD N = 57	Stunted Mean ± SD N = 08		
DEMOGRAPHIC PROFILE				
Age	9.51 ± 3.51	5.12 ± 2.94	3.363	**0.001****
CIRCUMFERENCE				
Mid Upper Arm Circumference	19.64 ± 1.98	14.68 ± 1.51	0.702	0.485
BLOOD PARAMETER				
Haemoglobin	12.47 ± 1.81	12.40 ± 1.79	0.103	0.918
Platelets	.994 ± .648	.847 ± .611	-604	0.548
Packed cell Volume	37.91 ± 4.57	38.60 ± 4.01	-0.404	0.687
Total Leucocyte count	4522.71 ± 1858. 5	4429.4 ± 2174.53	0.13	0.897
RENAL PARAMETER				
Urea	18.75 ± 6.36	22.25 ± 7.72	-1.418	0.161
Creatinine	.489 ± 0.126	.400 ± .106	2.732	**0.056***
LIVER PARAMETER				
SGOT	142.07 ± 136.9	117.50 ± 38.5	0.502	0.618
SGPT	63.96 ± 66.74	34.12 ± 7.24	3.241	**0.002*****
ALP	155.42 ± 49.24	131.38 ± 44.11	1.308	0.196

Values are expressed as Mean ± SD; p value calculated using independent student – t test, *p<0.05- ***p<0.01- statistically significant, ns- not significant,

Table 4 is based on the comparison of age, anthropometry and laboratory parameters with height. The number of children with dengue was significantly less in children who were stunted. It is found that children who are stunted had statistically less chance of elevated creatinine and their SGPT levels were also not raised to the extent in normal height children.

DISCUSSION

When we compared the nutritional status of the individual with severity of dengue, we have got some association but no statistical significance. We noticed that subjects with stunted height had more prevalence of shock and more stay in hospital as compared to their nutritionally healthy counterpart. In our study we found that 75% of children with undernutrition had need for PICU admission and 50% developed shock. We also noticed that underweight children had greater increase in the level of ferritin when compared to normal subjects. These findings were similar to the meta-analysis conducted by **Guzman MG et.al.** In this meta-analysis it was found that normal nutritional status may be a protective factor against DSS. 3

However, in contrast to our findings, **Kalayanarooj et al** found that malnutritional status may be a protective factor against development of severe Dengue fever.4 Of the 4,532 confirmed cases of dengue infection in the study, 80.9% were dengue hemorrhagic fever (DHF) and 19.1% were dengue fever cases (DF).

Among the DHF patients 30.6% had shock. The majority of them, 66.6%, had a normal nutritional status, while 9.3% were malnourished and 24.2% had obesity as classified by weight for age. Compared with control patients, malnourished children had a lower risk of contracting dengue infection (odds ratio = 0.48, 95% CI = 0.39-0.60, p = 0.000) while obese children had a greater risk of infection with dengue viruses (odds ratio = 1.96, 95% CI = 1.55-2.5, p = 0.000).

The clinical signs, symptoms and laboratory findings of dengue were almost the same among the 3 groups of malnourished, normal, and obese patients.

Similarly, in the study done in Thailand by **Sarunya et al** also, malnutrition was observed to be a protective factor against severe dengue.5 They observed in their study that children who were overweight had an increased risk of dengue severity (odds ratio (OR) = 1.76), 95% confidence interval (CI): 1.13–2.75, P = 0.012; OR = 1.84, 95% CI: 1.09–3.09, P = 0.022, per international and national growth criteria, respectively]. In addition, they found that stunting was associated with decreased risk of dengue severity (OR = 0.54, 95% CI: 0.33–0.88, P = 0.013)

Nguyen Thi Huyen et al in their systematic review and metanalysis on nutritional status and dengue infection found that association between nutritional status and severity of dengue infection were inconclusive. There was poor association of both overweight and underweight in severity of infection. 6 The analysis found that there was no statistically significant association between DHF group and DSS group in both patients with malnutrition and overweight/obese patients with OR: 1.17 (95 % CI: 0.99–1.39), 1.31 (0.91–1.88), respectively.

A significantly inverse relation between DF and DHF groups of malnutrition patients was revealed (OR = 0.71, 95 % CI: 0.56–0.90). The meta-analysis also indicated a statistically significant negative correlation between malnourished children with dengue virus infection and healthy children (OR = 0.46, 95 % CI: 0.3–0.70).

When analyzing patients with normal nutrition status, they found out that there was a significantly negative relationship between DHF and DSS groups (0.87; 95 % CI: 0.77–0.99). Other comparisons of DSS with DF/DHF groups, DSS/DHF with DF groups, and DHF with DF groups in normal nutritional patients showed no significant correlation.

A study done by **UsaThisyakorn et al** also concluded that severe cases of dengue are not undernourished which was contradicted by our study, as 75% of children with under nutrition had a prolonged stay in PICU and 50% developed shock too.7

Gabriela M. Marón et al concluded that excess nutrition does not appear to be a risk factor for severe forms of dengue infection in El Salvador, nor does malnutrition appear to be predictive of good outcomes which was similar to our study. 8

CONCLUSION

Although undernourished children are more likely to suffer from severe dengue, there was no significant correlation between nutritional status of child with the severity of dengue infection.

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