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Impact of Obesity on Shock of Dengue Hemorrhagic Fever Among Children at Tertiary Care Hospital of Bangladesh

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Abstract

Background: The association between nutritional status and dengue infection is still considered controversial. **Objective:** The purpose of the present study was to find out the relationship (association) between obesity and shock of dengue hemorrhagic fever (DHF) in pediatric patient. **Methodology:** This case-control study was conducted on children up to 14 years of age with dengue hemorrhagic fever admitted from May 2021 to November 2021 at the Pediatric Department of Evercare Hospital, Dhaka, Bangladesh. Data were analyzed after collection of demographic and clinical data of 71 enrolled children, out of which 40 DHF with shock and 31 DHF without shock. Overweight & obesity was assessed with BMI according to CDC growth chart. Statistical analysis of the results was obtained by using windows computer software with Statistical Packages for Social Sciences (SPSS-version 22). **Results:** Out of 71 patients, prevalence of DHF with shock is 56.3% and DHF without shock is 43.6%. Obesity was found 20(50%) in DHF with shock and 5(16.1%) in DHF without shock which showed statistically significant. Furthermore, pleural effusion (p=0.001), ascites (p=0.022), pulmonary oedema (p=.006), highest HCT > 46% (0.013%) also had significant association with shock event. **Conclusion:** There is significant relationship between obesity, pleural effusion, ascites, pulmonary oedema and highest hematocrit level with DHF with shock. Weak pulse was more common sign of shock followed by narrow pulse pressure, hypotension, cold clammy skin and decrease urine output. [*Bangladesh Journal of Infectious Diseases, December 2024;11(2):115-120*]

Keywords: Obesity; children; dengue shock; syndrome

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Introduction

Dengue fever (DF), a mosquito borne viral fever and its severe manifestations Dengue Haemorrhagic Fever (DHF) and Dengue Shock syndrome (DSS), is an increasing health problem with increasing global burden[1]. Asia region stands on the first ranks of dengue fever cases every year. In this country, Dengue hemorrhagic fever is still one of the significant public health problems. In Indonesia, Dengue Hemorrhagic Fever (DHF), occurred during 2019, a total of 18 cases with Incidence Rate

72/100,000 population. Their result shows that occurred in children aged 5-11 years old and male. Children are a vulnerable group to dengue virus infection related to their many outdoor activities that make them exposed to Aedes Aegypty[2]. In Thailand, dengue occurred in children aged five years and adults in 25 years. During 2000 and 2001, most cases in Thailand were dengue hemorrhagic fever (DHF) and Dengue Shock Syndrome (DSS) that attacked children at 5 and 14 years old[3]. In Malaysia, there were 10,000 cases of dengue every year and lead the country to suffer losses of US $13 million per year. This loss is equivalent to 940,000 working days lost[4].

As of 20 November 2022, a total of 52 807 laboratory-confirmed dengue cases and 230 related deaths have been reported by the Ministry of Health & Family Welfare of Bangladesh since 1 January 2022 with a case fatality rate (CFR) of 0.44%. Dengue is endemic in Bangladesh however a surge of cases started in June 2022. Currently, all eight divisions in the country are reporting cases and deaths. This is the second-largest outbreak since 2000, with the largest having occurred in 2019. The current dengue outbreak is unusual in its scale and seasonality[5].

According to the World Health Organization (WHO), DHF patients with dengue shock syndrome (DSS), have the most severe form of dengue infection[6]. Pathophysiology of DHF/DSS involves various inflammatory cytokines as as IL-6, IL-8, IL-10, TNF-α, MIF, VEGF, IFN-αβ and IFN-γ[7]. These cytokines affect vascular permeability and trigger plasma leakage. Research has shown that TNF-α synergize with dengue virus to modify adhesion molecule on endothelial cell and increases vascular permeability[8]. These cytokines would form 'cytokine storms' that will increase vascular permeability and cause vascular leakage[9]. Children were found to be more susceptible to shock than adults because of children have less well- developed mechanism in minimizing heart decompensation against increasing vascular permeability, thus making children more vulnerable to hemodynamic instability[10].

This finding could be explained because children have greater vascular permeability than adults, which makes them more vulnerable to vascular leakage during dengue infection[11]. Also in children, it required much less significant fluid loss to induce shock in their hemodynamic system compared with adults, thus explaining why children were more vulnerable to hypovolemic shock[12].

Obesity was initially thought to induce shock in DHF patients because adipose tissue expresses inflammatory cytokines such as TNF-α, IL-6, IL-8 and IL-1β, that may play a role in increasing vascular permeability and plasma leakage which led to DSS[13]. Many studies have discussed the relationship of obesity to shock in patients with DHF; those study showed that obesity is the risk factor of DSS. However, this relationship is still controversial given the many variations of the research design, as well as variables used in research[14-18]. Therefore, this research aims to find the relationship between the nutritional status on the outcome of pediatric patients with DSS.

Methodology

Study Settings and Population: This case-control study was conducted from May 2021 to November 2021 for a period of 6 months at the Pediatrics Department of Evercare Hospital. The hospitalized children aged up to 14 years, irrespective of sex with positive dengue tests, either NS1 antigen, IgM antibody or RT-PCR test were included in the study. Children with other bacterial & parasitic illness, neonate were excluded from the study.

Study Procedure: Purpose of the study was explained to the parents. Informed consent as obtained from all the parents before conducting the study. Dengue case classification by severity was done as per national guidelines of dengue fever Bangladesh 2019. This study enrolled a total of 71 hospitalized children aged up to 14 years who met WHO (2011) criteria for DHF or DSS admitted in Department of Pediatrics, Ever care hospital Dhaka. Study subjects were collected by using consecutive sampling. After enrollment of 71 children study subjects were divided in to 2 groups. First group, the case group included patient diagnosed with DHF with shock (grade III or IV), who meet the criteria of DHF plus sign of shock, such as weak pulse, narrow pulse pressure, poor tissue perfusion, clammy skin and decrease urine output according to WHO criteria.[22] Second group, the control group consists of subjects with DHF without shock (grade I or II), positive tourniquet test, 2 – 7 days of fever, thrombocytopenia and positive signs of plasma leakage such as increased hematocrit, or having pleural effusion, or ascites. Overweight & obesity was assessed with BMI according to CDC growth chart[20].

Statistical Analysis: Statistical analyses were carried out by using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were found with parametric distribution, presented as means ± standard deviations and tested by the Student t-test. The quantitative observations were indicated

by frequencies, percentages and Chi-Square test was done and showed with cross tabulation. P<0.05 was consider as statistically significant difference.

Ethical Clearance: All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., Helsinki Declaration) and also with the ethical guidelines of the Institutional research ethics. Formal ethics approval was granted by the local ethics com. Ethical clearance was obtained from the institutional ethics committee and informed written consent was taken from parents or caregivers of each enrolled child.

Results

A total number of 71 children were included in this study. Among them 40 (56.3%) of DHF with shock and 31 (43.6%) children of DHF without shock.

Table 1: Demographic Characteristics of The Study Subjects (n=71)

Variables	DHF		P value
	With Shock	Without Shock	
Age Group			
• ≤10 Years	20(50.0%)	12(38.4%)	
• >10 Years	20(50.0%)	19(61.6%)	
Mean ± SD	9.96±2.61	10.16±4.18	[a]0.805[ns]
Range (min-max)	4.5-14.8	0.4-14.9	
Gender			
• Male	25(62.5%)	17(54.8%)	[b]0.514[ns]
• Female	15(37.5%)	14(45.2%)	

ns= not significant; [a]p value reached from Unpaired-t test; [b]p value reached from Chi-square test

Table 2: BMI of the Study Subjects (n=71)

BMI (Kg/m^2)	DHF		P value
	With Shock	Without Shock	
• Underweight	3(7.5%)	1(3.2%)	
• Healthy weight	12(30.0%)	23(74.1%)	[b]0.011[s]
• Overweight	5(12.5%)	2(6.4%)	
• Obese	20(50.0%)	5(16.1%)	
Mean±SD	21.23±5.56	19.7±4.74	[a]0.224[ns]
Range (min-max)	12.2 to 30.7	12.2 to 33	

s= significant, ns= not significant, [a]p value reached from Unpaired-t test, [b]p value reached from Chi-square test

Age group more than 10 years was found more common (50%) in DHF with shock and 61.6% in DHF without shock. Almost two third (62.5%) patients were male in DHF with shock and 17(54.8%) in DHF without shock. The results of the analyses test found no association between age and gender (Table 1).

Obese was found 20 (50.0%) in DHF with shock and 5(16.1%) in DHF without shock, which showed statistically significant between two group (Table 2).

Moreover, other factors that might be related to shock events in DHF were also analyzed. We found that Pleural effusion was 22(55.0%) and 4(12.9%) in DHF with shock and without shock respectively. Ascites was found 13(32.5%) in DHF with shock and 3(9.7%) in DHF without shock. Pulmonary oedema was 11(27.5%) in DHF with shock and 1(3.2%) in DHF without shock (Table 3).

Table 3: Clinical features of the Study Subjects (n=71)

Clinical Features	DHF		P value
	With Shock	Without Shock	
Pleural Effusion			
• Yes	22(55.0%)	4(12.9%)	[b]0.001[s]
• No	18(45.0%)	27(87.1%)	
Abdominal Pain			
• Yes	20(50.0%)	9(29.0%)	[b]0.074[ns]
• No	20(50.0%)	22(71.0%)	
Ascites			
• Yes	13(32.5%)	3(9.7%)	[b]0.022[s]
• No	27(67.5%)	28(90.3%)	
Pulmonary Oedema			
• Yes	11(27.5%)	1(3.2%)	[b]0.006[s]
• No	29(72.5%)	30(96.8%)	
Hepatomegally			
• Yes	8(20.0%)	4(12.9%)	[b]0.428[ns]
• No	32(80.0%)	27(87.1%)	

s= significant, ns= not significant, [a]p value reached from Unpaired-t test, [b]p value reached from Chi-square test

Regarding the sign of shock, it was observed that weak pulse was more common followed by narrow pulse pressure, hypotension, cold clammy skin and decrease urine output (Table 4).

Table 4: Sign of Shock of the Study Subjects of DHF with Shock (n=40)

Sign of Shock	Frequency	Percent
Weak Pulse		
• Yes	39	97.5
• No	1	2.5
Narrow Pulse Pressure		
• Yes	23	57.5

Sign of Shock	Frequency	Percent
• No	17	42.5
Hypotension		
• Yes	19	47.5
• No	21	52.5
Cold Clammy Skin		
• Yes	13	32.5
• No	27	67.5
Decrease urine output		
• Yes	11	27.5
• No	29	72.5

ns= not significant, [a]p value reached from Unpaired-t test, [b]p value reached from Chi-square test

The mean highest hematocrit level was 43.41±4.42% and 40.67±4.6% in DHF with shock and without shock respectively. All are statistically significant ($p<0.05$) between two group (Table 5).

Table 5: Lab Findings of the Study Subjects (n=71)

	DHF		
Lab Findings	**With Shock**	**Without Shock**	**P value**
Highest Hematocrit Level			
• ≥46%	13(32.5%)	5(16.1%)	[b]0.115[ns]
• <46%	27(67.5%)	26(83.9%)	
Mean±SD	43.4±4.42	40.67±4.6	[a]0.013[s]
Range	31.4-50.5	30.6-53.1	
Lowest Platelet Count (10^3/L)			
• ≥50000	17(42.5%)	17(54.8%)	[b]0.302[ns]
• <50000	23(57.5%)	14(45.2%)	
Mean±SD	51.6±36.53	49.9±21.53	[a]0.825[ns]
Range	6 to 150	10 to 90	

s=significant, ns= not significant, [a]p value reached from Unpaired-t test, [b]p value reached from Chi-square test

Discussion

In this study we found that overweight or obesity is associated with shock in children with DHF. Similar result found in other study that, children with overweight/obesity were more prone to develop complications and even mortality because their immune systems were better than children with malnutrition. Thus, the immune reaction also became greater. In children with obesity, white adipose tissue (WAT) was increased, as well as in overweight, presumably. This finding was supported by the theory that obesity may affect the severity of dengue infection due to the increased production of white adipose tissue which causes increased inflammation mediator production. Obesity was associated with severity of dengue and therefore becoming a DSS risk factor[18].

In this present study, it was observed that pleural effusion, ascites and pulmonary oedema significantly associated with shock events. Similarly, in another study found that pleural effusion had a significant association with shock events.[18] However, abdominal pain and hepatomegally were more common in shock events but the difference was not statistically significant between DHF with shock and without shock. Although, several studies claimed abdominal pain and hepatomegaly as predictors of shock in children with DHF [16, 21, 22] .

Regarding the sign of shock, it was observed in this study that weak pulse was more common followed by narrow pulse pressure, hypotension, cold clammy skin and decrease urine output. In another study showed that there is decompensation, both systolic and diastolic BPs disappear suddenly and dramatically, and the patient is said to have hypotensive or decompensated shock. At this time the peripheral pulses disappear while the central pulse (femoral) will be weak. Hypotension develops when physiologic attempts to maintain systolic BP and perfusion are no longer effective. Hypotension is a late finding and signals an imminent total cardiorespiratory collapse.[23]

The World Health Organization (WHO) had classified DF and DHF based on clinical and laboratory values, with evidence of plasma leakage being the main difference between DF and DHF. Based on DHF criteria of WHO 2011, the main hematological parameters to differentiate DHF and DF are hematocrit rise ≥20% and thrombocyte level of <100,000/µl1. These findings are constant features of DHF.[6] Similar result found in a study mentioned that an increase in hematocrit describes the condition of hemoconcentration. Plasma leakage through the damaged blood vessels to the extravascular leads to an increased percentage of hematocrit consequent to deficiency in blood plasma related to blood viscosity.[24] In this study it was observed that the means highest hematocrit level was significantly ($p<0.05$) elevated in DHF with shock. However, lowest platelet count was almost identical between two groups.

In this study we found that highest hematocrit level was 43.41±4.42% related with shock similar result was found in other study where showed that the hematocrit level of ≥ 46% was related to shock in children with DHF[18]. Concurrent with other studies where found that hematocrit level could not be used as a shock indicator, cause those level was affected by spontaneous bleeding and also the administration of intravenous fluids. Massive bleeding could lower the hematocrit level, while dehydration and plasma

leakage could raise it instead[18]. In our country, one study reported that the degree of increase above the baseline hematocrit often reflects the severity of plasma leakage. Hemoconcentration, manifested by an increase in hematocrit of ≥20% above the baseline hematocrit may be seen. Clinicians should remember that a child with a low baseline hematocrit of 30.0%, presenting with dengue shock and a hematocrit of 40.0%, is relatively more hemo-concentrated than another child with a baseline value of 42.0% and a hematocrit of 50% at the time of shock[18].

Haematological analyses have been used for dengue diagnosis and severity classification in a variety of health-care settings, from primary to tertiary. In our study platelet count was not significantly associated with disease severity. But in contrast with other study where reported that platelet count was significantly associated with disease progression. Patients with low platelet count showing a higher risk of progressing to severe disease. This finding is consistent with the observed decrease in platelet counts recorded in other observational studies (Lam et al. 2017) and confirms platelet count as one of the key warning signs (WHO 2009) [25, 26, 27.]

This study has some limitations include small sample size, only one centre study, short duration of study period as well as sample was taken by purposive method, so there was chance of personal biasness.

Conclusion

There was significant relationship between obesity, pleural effusion, ascities, pulmonary oedema and highest Hematocrit level with DHF with shock. Weak pulse was more common sign of shock followed by narrow pulse pressure, hypotension, cold clammy skin and decrease urine output. In conclusion, observation and monitoring in overweight children with DHF should be done thoroughly because they were more prone to develop shock, which could lead to mortality. Furthermore, children with pleural effusion, hematocrit level of ≥ 46%, and platelet count of ≤ 50,000/μL were also at risk of developing shock.

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Conflict of Interest
None

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The individual contribution of the authors is given herewith: Ferdous J: Conceptualization; Methodology; execution; Investigation; Data collection; laboratory processing; Formal analysis and Interpretation; Writing- original draft; Writing- review and editing; Hassan Q: Data collection; Writing- original draft; Writing- review and editing; Sultana S: Formal analysis and Interpretation; Writing- original draft; Writing- review and editing; Zabeen F: Conceptualization; Methodology; Supervision; Reviewing and revising and editing. All of the listed authors have reviewed and approved the manuscript.

Data Availability
Any questions regarding the availability of the study's supportin g data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate
The Institutional Review Board granted the study ethical approval. Since this was a prospective study, every study participant provided formal informed consent. Each method followed the appropriate rules and regulations.

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