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Risk Factors of Death among Children with Dengue Hemorrhagic Fever

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ABSTRACT

Introduction: Dengue hemorrhagic fever (DHF) is still periodically around developing countries including Indonesia. Early diagnosis and adequate management may decrease either morbidity or mortality of patients with DHF.

Methods: We conducted a retrospective study by reviewing the medical records of children less than 18 years old hospitalized with DHF from January 2016 to December 2018. The diagnosis was based on WHO criteria and serologically positive anti-dengue Ig M or positive anti-dengue IgM and Ig G.

Results: During the study period, 70 patients aged 1-17 years with the complete medical records enrolled in this study. The DHF severity consisted of 37 cases (52.9%) with shock (DSS) and 33 cases (41. 7%) without shock and most of them were admitted to the hospital on >3 days of fever (63 cases /90.,0%). Boys were predominantly (39/55.,7%) found than girls (31/44.,3%) and the majority of cases above 5 years (50/71,4%) with well-nourished patients in 46 cases (65.,7%). The hematocrit level of≥ 40 mg/dl, platelets ≤ 40.000/mm^3, and leukocyte ≤ 4000 mm^3/l were observed in 41 cases (5.,6%), 36 cases (51.,4%), and 48 cases (68.,6%); respectively. Death was observed in four girls (5.7%) (p=0,034/OR 1,148/ 95% CI 1,003 - 1,315) with DSS because of severe conditions on admission.

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(Continued from previous page)

Conclusion: Our study found that death was mostly found in girls admitted to the hospital with late condition of dengue shock syndrome. Therefore, it is recommended for patients to early visit the primary healthcare facilities and be referred to the hospital for close monitoring and better management before the patients develop shock to decrease the mortality rate of patients with DHF

Keywords: Risk factor; death; dengue hemorrhagic fever; children

Introduction

Dengue and DHF are still endemic in Africa, the Americas, the Eastern Mediterranean, South-East Asia and the Western Pacific. An estimated 50 million dengue infections occur worldwide annually and approximately 500,000 hospitalized cases with DHF, particularly in children. [(1)]

Children with severe DHF maybe falling into DSS event death if inadequately managed.[(2,3)]An approximately 90% of them are children aged less than five years and about 2.5% of the affected children die.[(4)]

Despite, prevention and control programs of DHF performed on a national scale by the Ministry of Health of Indonesia since 1968, there was an increase in the annual incidence rate of DHF in Indonesia, from 0.05 cases per 100,000 person-years in 1968 to 77.96 cases per 100,000 person-years in 2016 and in 2017, there were 59,047 and 444 of DHF cases and DHF-associated deaths; respectively, with case fatality rate of 0,75%. [(5)]

Therefore, we aimed to retrospectively review the death of DHF patients aged ≤ 18 years old hospitalized in Wahidin Sudirohusodo Hospital Makassar.

Methods

We conducted a retrospective study by reviewing the medical records of children less than 18 years old hospitalized with DHF from January 2016 to December 2018. This study was approved by the Institutional Review Board of the Wahidin Sudirohusodo Hospital Makassar.

Patients with complete medical records during the study period were collected and reviewed. DHF was diagnosed based on WHO criteria guidelines and serologically positive anti-dengue Ig M or positive anti-dengue IgM and Ig G by ELISA technique were included in the present study. [(6,7,8,9)] The patients with comorbidities and incomplete medical records were excluded from the study.

Diagnosis of DHF was clinically based on 1) fever 2-7 days, 2) bleeding manifestations such as positive tourniquet test, petechiae, ecchymoses, bleeding from the mucosa, gastrointestinal tract, or other locations, 3) thrombocytopenia (platelet count < 100,000 /mm^3), 4)evidence of plasma leakage manifested as elevated hematocrit level > 20% from baseline or > 40%. Severity of DHF was adedas 1) Grade-I, if DHF with positive tourniquet test, 2) Grade-II, if spontaneous bleeding exists in addition to the manifestations of grade-I, 3) Grade-III, if evidence of circulatory failure manifested by a rapid, weak pulse and pulse pressure < 20 mmHg or hypotension for age with the presence of cold, clammy skin and restlessness, and 4) Grade-IV: Profound shock with undetectable blood pressure or pulse. Leukopenia was defined as leukocyte count <4000 mm^3/l); hemoconcentration was confirmed by elevated hematocrit level > 20% from baseline or > 40%or progressive increased periodically, and thrombocytopenia was established if the platelets count <100,000 mm^3/l (6,7,8) The laboratory investigations on admission were all performed at Wahidin Sudirohusodo Hospital laboratory including anti-dengue Ig M and Ig G, hematocrit level, platelets count, and leukocyte count.

Nutritional status was based on WHO (body weight/body height SD) criteria, categorized as well-nourished { (>90 / (+2 SD) – (- 2 SD)}, poorly-nourished { (< 70 / (- 3 SD), and overweight ({ (>100 / (>+ 3 SD) – (+ 3 SD)}.(10)Data of patients collected from the medical records including age, sex, nutritional status, duration of fever, grading of DHF, hematocrit level, platelets count, white blood cells, and outcome of patients.Data of the enrolled patients was collected and analysed with SPSS 21. A chi-square, Fisher's exact test, crude odds ratio (OR), and 95% confidence interval (95%CI) was used to determine the risk factors of death. A p-value < 0.05 was considered statistically significant.

Result

During the study period, 70 patients aged 1-17 years with the mean age of 8,17 years (SD4,47) were enrolled in this study. The DHF severity consisted of dengue shock syndrome in 37 cases (52,9%) and another 33 cases (41,7%) of DHF without shock. Boys were predominantly (39/55,7%) encountered than girls (31/44,3%) with mostly of the cases was observed in patients>5 years (50/71,4%) and 0 – 5 years in 20 cases (28,6%). Nutritional status of the patients in this study was mostly in well-nourished (46 cases/65,7%), followed by poorly-nourished 13/18,6% and overweight 9/12,9%. Most of the patients entered the hospital with fever >3 days (63 cases/90,0%) and ≤ 3 days in 7 cases (10,0%). Laboratory features of the patients were elevated hematocrit level of ≥ 40 mg/dl in 41 cases (58,6%) ranged from 38.20 to 49.00 % with the mean of 42.07% (SD 2.91) and the median of 41.00%, platelets count ≤ 40.000/mm^3in 36 cases (51.4%) ranged from 6000 to 98000 cells/mm^3 with the mean of 40.500, cells/mm^3 (SD 24757.81) and the median 35500.00 cells/mm3., and leukocyte count≤4000 mm^3/l in 48 cases (68,6%)ranged from 1600 to 5890 cells/mm3 with the mean of 3727,85 cells/mm3 (SD 890.378) and the median of 3700,00 cells/mm3.We observed 66 cases

(94,3%) were alive and 4 cases (5,7%) passed away all of them being girls with dengue shock syndrome baseline data of the patients shown in Table 1.

According to the statistical analysis, death was observed significantly in 4 girls (5,7%) with dengue shock syndrome (p0,034//OR 1,148/ 95% CI 1,003 - 1,315). We suspect that death in those patients were admission to hospital accompanied with severe condition. The outcome of children with DHF were shown in table 2.

Discussion

Seventy (70) patients with DHF hospitalized from2016 to 2018were enrolled in this study. Our observation revealed that boys predominantly (39/55,7%) suffered from DHF than girls (31/44.3%) with the most cases being in children > 5 years (50/71,4%). Faridi MA et al. also showed 76 % of all their patients aged ≥ 6 years old (11) and nearly similar to others observing DHF in patients aged 5 to 10 year old.(9,12) Sahana KS et al. documented that boys was slightly more affected than girls (12)as well as a study by Athira PP et el.34 cases(59,0%)on boys.(13)The average age of our patients was 8.17 ± 4.47 and almost similar to a study by Athira PP et al.(7.6 years ± 4.8).(13)

In the present study, the elevated hematocrit level > 40 mg/dl were found in 41 cases (58.6%), the platelets count<40000/mm^3 in 22 cases (31.4%), 40000- 98.000/mm^3in 48 cases (68.6%), and leukocyte count≤ 4000 mm^3/l in 48 cases (68,6%); respectively. The above three laboratory features may be considered as important clues to support the diagnosis of DHF. Faridi MA et al.(11)and Aggarwal A et al.(14) also reported the similar findings. Mittal H et al. documented that a positive tourniquet test and leukopenia are helpful in making early diagnosis of dengue infection with a positive predictive value of 70%–80%.(15)In our study, the anti-dengue Ig G and/or Ig M were positive in all patients for detection of dengue infection, which was almost similar to some previous studies.(16,17)

Although most of patients were alive, unfortunately4 girls (5.7%) died due to admitting to the hospital with the late phase of Dengue shock syndrome. Dhooria GS et al. noted that all of death in DHF patients belonged to DSS.(18)Our figure of death was relatively higher than Ahmed et al.(19)and Faridi MA et al.(11)observing death of 3% and 3.7%cases ; respectively and less than 6% cases of death studied by Agrawal A et al.(14)All of the death among DHF patients may be due to delayed diagnosis of subsequently management of patients with DHF.

Limitation

A major limitation of our study is that it is a retrospective study with secondary data collected from the medical records. This may draw the possibility of record bias and the data obtained were only from a single hospital. However, this study can be an important issue for the next multicentre hospital studies.

Conclusion

Our study found that death was mostly found in girls admitted to the hospital with late condition of dengue shock syndrome. Therefore, it is recommended for patients to early visit the primary healthcare facilities and be referred to the hospital for close monitoring and better management before the patients develop shock to decrease the mortality rate of patients with DHF. Further prospective study design in multicentre hospitals and a larger number of subjects are needed.

Table 1. Baseline Data among Patients with DHF

Variables	Patients	
	Total	%
Age (years)		
Range 1-17		
Mean 8,17 (SD 4,47)		
Median 8,5		
0-5	20	28,6
> 5	50	71,4%
Sex		
Boys	39	55,7%
Girls	31	44,3%
Nutritional status		
Well-nourished	46	65,7%
Poorly-nourished	13	18,6%
Overweight	9	12,9%
Duration of fever (days)		
≤ 3	7	10,0%
>3	63	90,0%
Leukocyte counts(cells/mm3)		
Range 1600 - 5890		
Mean 3727,85(SD 890.378)		
Median 3700,00		
≤ 4000	48	68,6%
> 4000	22	31,4%
Platelets counts (cells/mm3)		
Range 6000 - 98000		
Mean 40500 (SD 24757.81)		
Median 35500.00		
≤ 40.000	22	31,4%
> 40.000	48	68,6%
Hematocrit level (%)		
Range 38.20-49.00		
Mean 42.07 (SD 2.91)		
Median 41.00		
> 40	41	58,6%
≤ 40	29	41,4%
DHF severity		
Shock	37	52,9%
No shock	33	47,1%

Death		
Yes	4	5,7%
No	66	94,3%
Total	70	100,0%

Table 2. Risk factors of death among patients with DHF

Variables	Death		Total (n/%)	P value	OR	95% CI
	Yes (n/%)	No (n/%)				
Age						
• 0-5 years	1/25,0	19/28,8	20/28,6	1,000	,825	,081 - 8,433
• > 5 years	3/75,0	47/71,2	50/71,4%			
Sex						
• Boys	0/0.0	39/59.1	39/55,7	0,034*	1,148	1,003 - 1,315
• Girls	4/100,0	27/40,9%	31/44,3			
Nutritional status						
• Good	2/50,0	46/69,7	48/68,6	,062	NC**	NC**
• Malnutrition	0/0.0	13/19,7	13/18,6			
• Overnutrition	2/50,0	7/ 10,6	9/12,9			
Duration of fever						
• ≤ 3 days	0/0.0	7/10,6	7/10,0	1,000	1,068	1,001 - 1,139
• >3 days	4/100.0	59/89,4	63/90.0			
Leukocyte counts						
• ≤ 4000	1/25,0	42/63,6	43/61,4	,291	,190	,019 - 1,934
• > 4000	3/75.0	24/36,4	27/38,6			
Platelets counts						
• ≤ 40.000	4/100.0	44/66,7	48/68,6	,301	,917	,842 - ,998
• > 40.000	0/0.0	22/33,3	22/31,4			
Haematocrit level						
• > 40	1/25,0	40/60,6	41/58,6	,300	,217	,021- 2,197
• ≤ 40	3/75.0	26/39,4	29/41,4			
DHF severity						
• Shock	4/100.0	33/50.0	37/52,9	,117	,892	,797 - ,998
• No shock	0/0.0	33/50.0	33/47,1			
Total	4/5.7	66/94.3	70/100.0			

*Significant p-value. ** NC = not calculated

Conflict of interest

None

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