ORIGINAL ARTICLE

Some Clinical and Epidemiological Observations on Virologically Confirmed Dengue Hemorrhagic Fever

by

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Abstract

This study is a part of a one year prospective study on dengue hemorrhagic fever (DHF) carried out in the Department of Pediatrics, Sumber Waras Hospital in West Jakarta. Viral isolation and serologic analysis for DHF were done by Namru-2 in Jakarta. The subjects were 151 virologically confirmed DHF Patients admitted to the Department of Pediatrics during the period of September 1987 - June 1988, consisting of 82 boys and 69 girls of 6 months - 15 years old.

The predominant age group was 5 to 9 years, representing 49.7% subjects. Dengue virus was isolated from sera during the first 8 days of illness and in 139 (42.1%) during the first 5 days of illness. Dengue virus type 1, 2, 3 and 4 were isolated from 16.6%, 13.2%, 69.5% and 0.7% subjects, respectively.

The clinical manifestations revealed no striking differences between dengue 3 and others except for thrombocytopenia and shock. High fever, hemoconcentration and thrombocytopenia on admission was observed in 30.5%, 8.6% and 8.6% of subjects, respectively.

Dengue shock syndrome (DSS) were observed in 23 (15.2%) with 3 (2%) fatal cases. Dengue virus serotype 3 was observed in 20 out of 23 DSS cases (86,9%) and all fatal cases were associated with dengue type 2.

This study revealed that dengue 3 is the predominant virus circulating during recent epidemics and is associated with more severe clinical manifestation and with a higher incidence rate of living area.

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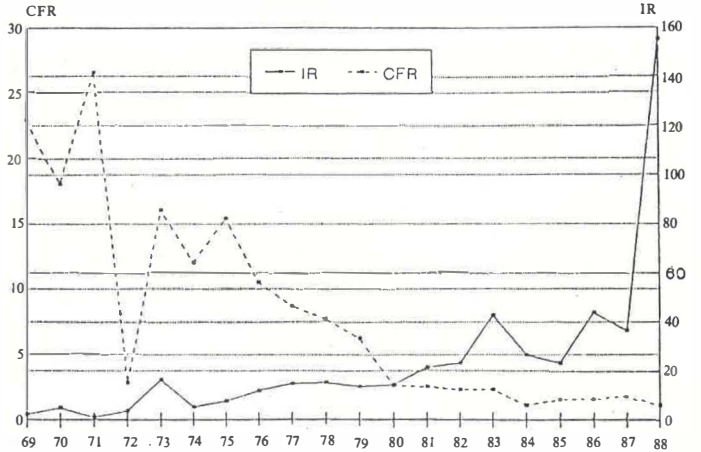
Introduction

Since the outbreak of Dengue Hemorrhagic Fever (DHF) in 1968, the disease has now become endemic with cases occurring through the year and it becomes one of the major public health problems in Indonesia. Epidemics of large proportion has been reported in the year of 1973, 1983 and 1985 (Suroso and Bang, 1985).

In Jakarta metropolitan the incidence rate of DHF is increasing sharply while the case fatality rate has declined to less than 2% since 1980 (Suroso, 1987) and the pattern of epidemics has become irregular with the tendency of shorter intervals between epidemics (Figure 1).

Figure 1 : *Incidence and case fatality rate DHF in Jakarta Metropolitan (1969-1988)*



IR = Incidence rate
CFR = Case fatality rate

(Source: Municipal Health Centre of Jakarta Metropolitan)

Virologic surveillance by virus isolations revealed that all four dengue serotypes are circulating in Jakarta but dengue 3 is the predominant virus isolated (Gubler et al., 1976 a: Sumarmo et al., 1986; and Muslim et al., 1988). It has also been reported that dengue 3 is associated with severe and fatal cases of DHF (Sumarmo et al., 1983). During dengue epidemics in Bantul in Central Java in 1976 dengue 3 was responsible for over 60% of the isolations (Gubler et al., 1979).

A changing pattern of virus isolations was observed in 1975 in the Pediatric Department, Cipto Mangunkusumo General Hospital in Jakarta where dengue 2 was the predominant virus isolated (Muslim et al., 1988).

In the second half year of 1987 an increasing cases of DHF were admitted to our department indicating that an epidemic is coming to occur and hence a one year prospective study starting from September 1987 was conducted in the Department of Pediatrics, Sumber Waras Hospital with the purpose to define the predominant virus circulating during recent epidemics and observe some of its clinical and epidemiologic aspects.

This report describes the preliminary findings of the study.

Materials and Methods

All subjects were admitted to the Department of Pediatrics, Sumber Waras Hospital in West Jakarta, during the period of September 1987 - June 1988. Detailed clinical records of each patients including the name, sex, age, home address, parents address of occupation, school, date of admission, date of onset of illness and clinical history werekept. On admission all patients were thoroughly examined for signs and symptoms suggestive of DHF including the tourniquet test.

The clinical diagnosis and the severity of DHF were graded based on the criteria as outlined by the WHO (1986).

Routine hemogram, urinalysis and occult blood in stool were performed on all patients. Serial determination of hemoglobin, hematocrit and platelets were taken daily or as frequent as every 4 hours in severely ill patients. Other laboratory analysis were done as indicated.

Virus isolations were attempted from the acute sera of all patients and were inoculated in Toxorynchites splendens and TRA 284 (T amboinensis) cells. Virus isolations and serologic analysis for DHF were carried out in Namru 2, Jakarta Detachment in Jakarta, Indonesia.

Results

It was evident that during the first 8 months of the study an epidemic of large proportion was occurring in Jakarta. From September through June 1988, 151 dengue virus has been isolated from 1.051 patients admitted with the clinical diagnosis of DHF, although culturing is not complete. About 68% of virus isolations was obtained from sera taken between 2 days - 4 days of illness and 92% from sera taken during the first 5 days of illness (Figure 2).

Virus serotype and age distribution

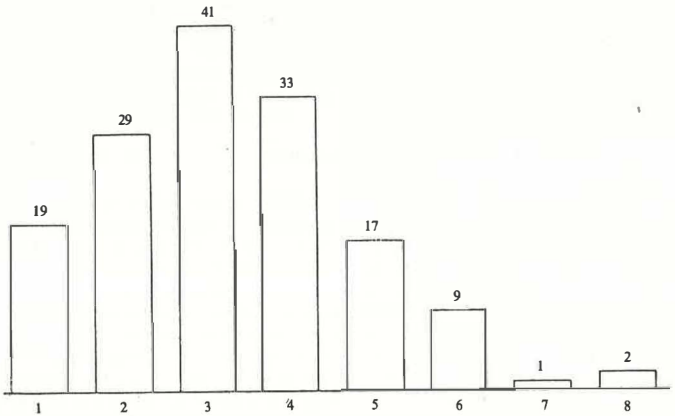
Dengue serotype distribution and age distribution are presented in Tables 1, 2 and Figure 3.

It was evident that the predominant age group was 5 years 9 years and dengue 3 was responsible for 69.5% of virus isolations. Statistically no significant difference in dengue virus distribution by age group was observed ($p > 0.05$).

Clinical manifestations

The clinical manifestations revealed no striking differences among dengue and other serotypes except for thrombocytopenia and shock (Table 4).

Figure 2 : *Viral isolations by days of illness*



(RSSW 1987 - 1988)

Table 1 : *Age distribution in virologically confirmed dengue hemorrhagic fever (RSSW, 1987 - 1988)*

Age (Years)	Dengue Serotype		Total
	D 3	D 1, 2, 4	
4	13 (12.4%)	8 (17.4%)	21 (13.9%)
5 - 9	54 (51.4%)	21 (45.7%)	75 (49.7%)
10 - 14	32 (30.5%)	15 (32.6%)	47 (31.1%)
15	6 (5.7%)	2 (4.3%)	8 (5.3%)
Total	105 (100%)	46 (100%)	151 (100%)

X^2 =

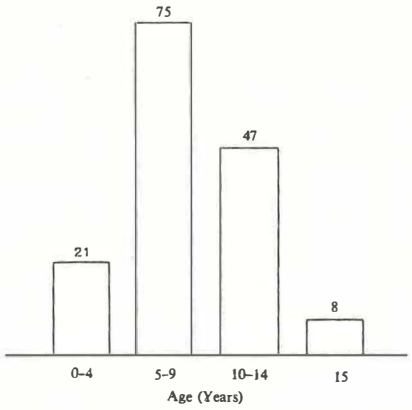
Table 2 : *Dengue virus distribution by sex and age among 151 virologically confirmed DHF (RSSW. 1987 – 1988)*

Age (Yrs)	Sex	Dengue Serotype				
		D1	D2	D3	D4	Total
< 1	M	–	–	1	–	1
	F	–	–	–	–	0
1 – 4	M	3	2	7	–	12
	F	0	3	5	–	8
5 – 9	M	4	7	26	–	37
	F	7	2	28	1	38
10 – 14	M	7	3	15	–	27
	F	2	3	17	–	20
≥ 15	M	1	–	4	–	5
	F	1	–	2	–	3
Total	M	15	12	55	–	82
	F	10	8	50	1	69
M + F	25	20	105	1	151	
	(%)	(16.2)	(13.2)	(69.5)	(0.7)	

High fever (≥ 39°C) was observed in 98 patients and in 46(30, 5%)of them the fever developed before admission. Hemoconcentration was observed in 66 patients (43,7%) and in 35,1% occurred in 2 days – 5 days of illness. Thrombocytopenia was observed in 58 patients, occurring in 3 – 5 days of illness in 42 (72.4%) of them. Thrombocytopenia on admission was observed in 13 (8,6%) patients

Dengue shock syndrome (DSS) was observed in 23 (15.2%) cases and fatal cases in 3 (2%) patients (Table 4). It is evident from Table 3 and 4 that dengue 3

Figure 3 : *Age distribution of 151 virologically confirmed DHF*



was associated with severe cases of DHF when compared with other dengue serotypes ($p < 0.05$). Shock on admission was observed in 13 (56.5%) patients. Shock developed during the first 6 days of illness and 18 (78.3%) between 2 - 5 days of illness.

Table 4 : *Severe cases by dengue serotype in verologically confirmed dengue hemorrhagic fever (RSSW, 1987 - 1988)*

Dengue Serotype	Total Cases	DSS Cases	Fatal Cases	
D1	25	2 (8.0%)	-	
D2	20	1 (5.0%)	-	
D4	1	-	-	
D1, 2, 4.	46	3 (6.5%)	-	
D3	105	23 (15.2%)	3	$0.05 > p > 0.01$
Total	151	23 (15.2%)	3 (2.0%)	

Table 3 : *Clinical manifestations by dengue serotype among virologically confirmed dengue hemorrhagic fever (RSSW, 1987 - 1988)*

Signs and Symptoms	Dengue serotype					Total
	D3	Others				
	105	D1 (25)	D2 (20)	D4 (1)	Total (46)	(151)
History of Bleeding	30	7	5	0	12	42
Abdominal Pain	42	9	8	1	18	84
High Fever ($\geq$ 39°C)	70	18	10	0	28	98
Tourniquet Test (+)	59	14	13	1	28	87
Spontaneous Bleeding	30	4	10	0	14	44
patomegaly	60	12	8	0	20	80
Hemoconcentration	45	14	7	0	21	66
Thrombocytopenia*	48	6	4	0	10	58
Shock*	20	2	1	0	3	23
Convulsions	6	0	0	0	0	6
Encephalopathy	4	0	1	0	1	5

* $p < 0.05$

Virus distribution by living area

Sumber Waras Hospital is located in and as a referral hospital for West Jakarta, most of the patients admitted to the Department of Pediatrics come from West and North Jakarta and some from Central Jakarta. The incidence rate of DHF in Jakarta Metropolitan during the period of 1982-1986 was 23-45/100.000 population. During this period only a few of the subdistricts had the DHF incidence rate of 80/100.000 population or more (Figure 4).

During recent epidemics the incidence rate (in each village) ranged from 0 - 650/100.000 population with the mean incidence rate of 155 ± 6.9/100.000 population. Table 5 shows the dengue virus distribution by the incidence rate of living area of the subjects. It was evident that the percentage of dengue 3 isolations was higher in living area of higher incidence rate as compared with titer dengue virus and the difference was statistically significant.

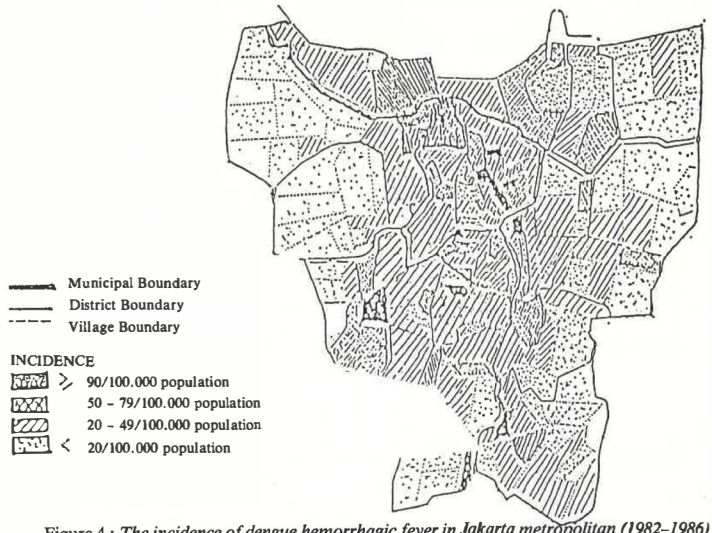


Figure 4 : *The incidence of dengue hemorrhagic fever in Jakarta metropolitan (1982–1986)*

Table 5 : *Dengue virus distribution by incidence rate among virologically confirmed dengue hemorrhagic fever*

Incidence rate (per 100.000 pop)	Dengue serotype		Total
	D3	Others	
100	3 (2.8%)	6 (13.0%)	9 (5.9%)
100 - 199	49 (46.7%)	18 (39.1%)	67 (44.4%)
200	53 (50.5%)	22 (47.8%)	75 (49.7%)
Total	105	46	151

$X^2 = 6.2187 \quad p < 0.05$

Discussion

A study in the duration of viremia in DHF revealed that viremia lasted for 4–5 days of illness (Gubler et al., 1976 b). The present study revealed that 92% of virus isolates were obtained from sera collected during the first 5 days of illness.

Although a changing pattern of dengue serotype was observed in 1985–1986 (Muslim et al., 1988) the predominant virus circulating during present and previous epidemics was dengue 3 (Gubler et al., 1976, 1979; Sumarmo et al., 1986). The WHO diagnostic criteria of DHF includes 4 cardinal signs (fever, hemorrhagic manifestations, hepatomegalia and shock) and 2 laboratory findings (hemoconcentration and thrombocytopenia). In Thiland where dengue 2 is predominant, hepatomegaly was observed in 80%–90% subjects (Nimanitya, 1969). It was thought that dengue 2 infections was associated with a higher percentage of hepatomegaly. In present epidemics and previous study in Jakarta (Sumarmo et al., 1986; Sidharta, et al., 1987) hepatomegaly was observed in 46%–53% of subjects. No significant difference was observed in the percentage of hepatomegaly by dengue serotypes.

Abdominal pain is not included in the WHO diagnostic criteria of DHF and yet this complaint compelled special attentions since it was associated with clinically more severe manifestations (Sumarmo et al., 1983) especially in children of 5 years old and more (Samsi and Susanto, 1987).

Present and previous studies (Sumarmo et al., 1983, 1986) revealed that dengue 3 was associated with more severe clinical manifestations and fatal cases, however the clinical signs and symptoms of dengue 3 and other dengue virus were statistically not different except for thrombocytopenia and shock. This study revealed that dengue 3 was associated with living area of higher incidence rate.

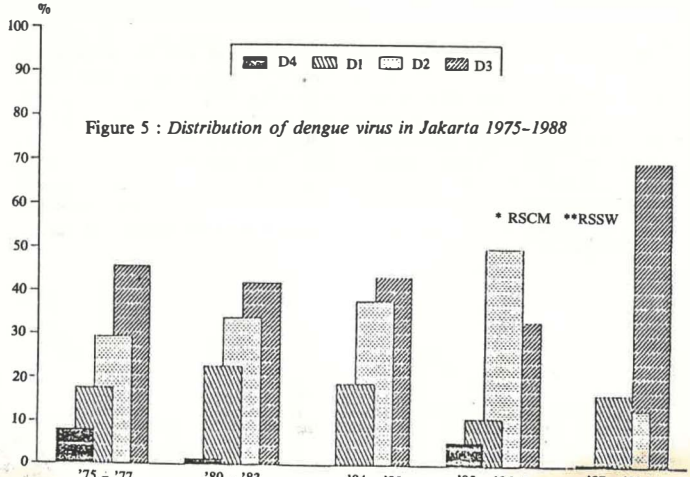


Figure 5 : *Distribution of dengue virus in Jakarta 1975–1988*

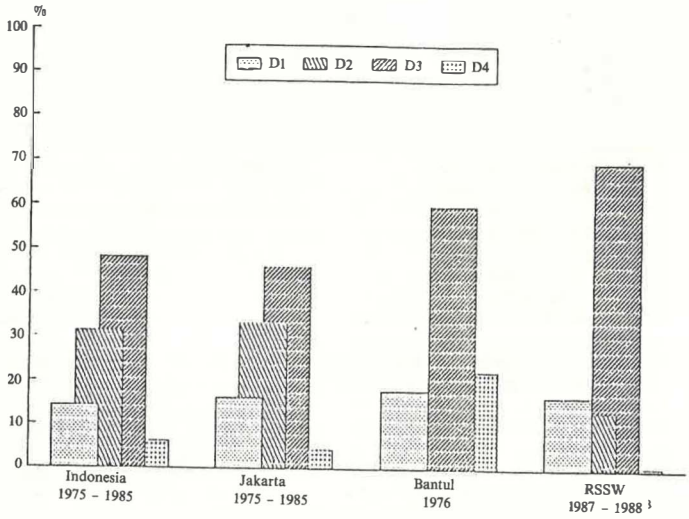


Figure 6 : *Distribution of dengue virus serotype in Indonesia*

Dengue virus distribution in Jakarta during the period of 1975-1985 and in recent epidemics is presented in Figure 5. The percentage of dengue 3 during epidemics was significantly higher than non epidemic ($p < 0.01$). The above situation is then compared with the situation in Indonesia and that of Bantul (Central Java) during the epidemic in 1976. These can be seen in Figure 6.

It is evident that the percentage of dengue 3 is higher during epidemics. It seems that dengue 3 plays an important role during epidemics in Jakarta metropolitan. Whether dengue 2 and others have their own epidemic pattern of a lesser magnitude and dengue 3 is responsible for epidemics of large proportion in Indonesia, further studies are needed.

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