

Mosquito-borne Haemorrhagic fever

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MOSQUITO-BORNE HAEMORRHAGIC FEVER

A study of 45 positive cases seen in the Paediatric Wards General Hospital, Kuala Lumpur. (May – September, 1973).

Introduction

This was the second epidemic of Haemorrhagic Fever observed in Malaysia. The first epidemic comprising of 61 cases occurred in Peninsular Malaysia in 1962. In that epidemic there were 14 isolates and they were identified as Dengue Type 11 (Rudnick et al – 1965). Since then only a few sporadic and isolated cases have been observed till May 1973. As the physicians were aware of this disease at the beginning of the second epidemic, the disease was identified fairly rapidly in its early stage.

Aetiology

Virus isolation

In the present study viruses were isolated from the acute phase sera of 4 patients. The method used for the isolation of virus is by inoculation of acute serum into the brains of suckling mice. Two of these isolates have been identified as being Dengue Type III virus.

In addition to the 4 cases where virus isolation had been successful 35 other cases showed significant

rises in group B arbovirus antibody titre by the haemagglutination – inhibition test. The method used for the detection of antibody rise in the second specimen of serum when compared to the acute phase (first) serum is according to the method of Clarke and Casals (1958). In 3 of the remaining cases it was necessary to make a presumptive diagnosis based on the significantly high levels of antibody in one specimen of serum. In all these 3 cases antibody titres to group B arbovirus of 1/1280 or greater were demonstrated. These titres were well above those studied in a group of normal children in Kuala Lumpur. Based on this study it was felt, with some justification, that these 3 cases should be included. In the remaining 3 other cases only 1 specimen of serum from each were available as they died early. 2 of these cases had low antibody titres to group B arboviruses a titre of 1/640 was demonstrated. On strong clinical grounds, however, it was felt that diagnosis of haemorrhagic fever should be made, although its aetiology could not be established with certainty, and that these 3 cases should also be included. Acute phase serum specimens should be taken within the first three days of disease in order to isolate virus and to demonstrate a rise in antibody titres when compared to a later specimen. However, many patients were not admitted into hospital until after the 3rd day of disease or were discharged after successful management but did not return for the

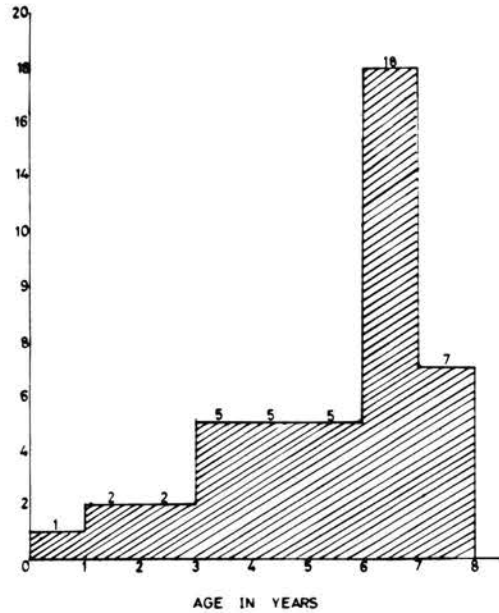
AGE DISTRIBUTION

collection of a 2nd specimen, hence no second specimens were obtained.

As the majority of these cases had originated from Jinjang village which is located on the fringe but within the boundary of Kuala Lumpur district, a mosquito survey was carried out. Larvae survey was carried out and it revealed an *Aedes* index of 71.9%. This is considered high but adult surveys did not reveal a very high abundance of *Aedes aegypti* or *Aedes albopictus*. Subsequent investigations carried out, strongly indicate that this was as an *Aedes aegypti* transmitted dengue infection.

Selection of cases

This is an analysis of 45 cases of Haemorrhagic Fever admitted to the childrens' ward, General Hospital Kuala Lumpur from May - September, 1973. Out of these 45 cases were confirmed as positive cases, 3 by direct isolation; 1 by direct isolation and serology and 41 by Haemagglutination inhibition studies. Only children below the age of 8 years are admitted to the Paediatric Wards in this hospital. (During this period a total 131 children were admitted to wards as suspected cases and blood sent for virological studies). There were 6 deaths among these cases.



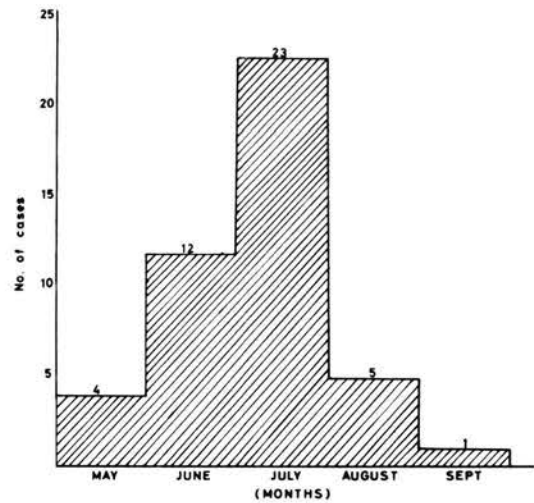
Racial distribution

Chinese 42, INdians 3, Malay Nil.

Area

The majority of the Chinese children came from the crowded suburb of Jinjang.

Jinjang 25, Ulu Selangor 6, Kuala Lumpur 8, Suburbs 11, Kajang 2, and Sabak Bernam 1.



Sex distribution

Male 19, Female 26.

The majority of the children i.e. 18 cases were between 6 and 7 years of age. There was only one case below the age of one year.

The maximum number of cases i.e. 23 occurred in the month of July.

Grade of disease according to severity. (based on classification used in the Bangkok Paediatric Dept: Ramathibodi Hospital).

DISTRIBUTION OF CASES IN VARIOUS MONTHS

Table 1

Grade I	Fever and mild symptoms but no frank bleeding.	5
Grade II	Significant bleeding from any site but no shock; including flushing of patients extremities or of the whole body.	29
Grade III	Shock or impending shock as shown by narrow pulse pressure of 20 mm.Hg. or less, hypotension with BP systolic 80 mm. Hg. or unobtainable BP.	11

Table 2

Clinical features	45 cases	
	%	No.
Fever	100	45
Bleeding tendency	66	30
Skin rashes	60	27
Hepatomegaly	55	25
Grade I		1
Grade II		15
Grade III		9
Vomiting	49	22
Injected throat	49	22
Abdominal pain	47	21
Lethargy	35	16

Table 3

Clinical features	45 cases	
	%	No.
Cough	33	15
Restlessness	27	12
Shock	25	11
Lymphadenopathy	22	10
Neck stiffness	11	6
Muscular pain	9	4
Convulsions (Death)	6	3
Death		2
Facial palsy	2	1
Distended bladder	2	1
Pleural effusion	2	1

Tables 2 and 3 show the clinical features in order of frequency.

Fever was the commonest feature seen and occurred in all cases. In 11 cases the fever lasted for 5-6 days. In 9 cases the fever lasted for 4-5 days and in 6 cases for more than 9 days. The majority had a low grade fever of about 100 – 101°F. Only 3 cases showed a temperature of above 102°F. Eleven cases developed shock, and these had the worst prognosis. All the 6 deaths were among cases who went into shock. Convulsions in 3 cases, 2 of whom died. Pleural effusion was seen in 1 case. This child showed remarkable improvement after pleural tapping was done.

Table 4

Total No. of cases	%	Cases
	66	30
Epistaxis	27	12
Melaena	24	11
Haematemesis	18	8
Gum bleeding	29	13
Hess Test positive (Grade III)	49	22 2 out of 11 cases.

BLEEDING TENDENCIES

Table 4 shows the type of bleeding tendencies seen in the 45 cases. 22 cases showed a positive Hess Test. However only 2 out of 11 cases in Grade III showed a positive Hess Test. This shows that in the presence of shock, this is not a reliable sign.

Table 5

Total No. of cases	%	Cases
	60	27
1. Flush	8.9	4
Generalised		2
Extremities		2
2. Erythema (maculopapular)	18	8
Generalised		4
Extremities		1
Face and trunk		3
3. Petechiae	35	16
4. Ecchymoses	6	3

SKIN LESIONS

Table 5 shows the different skin lesions. The flush seen was a diffuse violaceous flush, and at times a diffuse morbilliform rash. In a few cases there was an extensive maculopapular rash similar to that seen in measles.

LABORATORY RESULT:

	Grade 1		
	% No. out of 5 cases	% No. out of 29 cases	% No. out of 11 cases
50,000	1	6	6
50,000 - 100,000	2	16	3
100,000 - 200,000	2	5	1

Total white cell and differential count

PROGRESS OF THE DISEASE:-			
45 Patients:-	Stage I -	5	
	Stage II -	29	
	Stage III -	11	
MORTALITY -	6 cases (all in Grade III)		
Mortality cases:	P.M. in 3 cases		
Name of Patients	Duration of illness.	Duration of stay in Hospital	
1. Tan Pah Hong	4 days	21 hours	
2. Yap Yoke Ying	4 days	14 hours	
3. Pang Saw Mooi	9 days	2 days	
4. Soon Wan Hua	5 days	13 hours	
5. Wong Soon Moi	7 days	10 hours	
6. Yap Foo Keong	4 days	1 hour	

PLATELET COUNT -- 42 done

	Grade I 5 cases	Grade II 29 cases	Grade III 11 cases
Serum albumin		3.2 gms	3.55 gms
Total protein		5.4 gms	5.6 gms
SDT	76 units	105 units	311 units
SGPT	23 units	57 units	212 units

CORRELATION OF LIVER FUNCTION TESTS TO SEVERITY OF DISEASE

This table shows the lowest values obtained for Serum albumin and Total Protein, and the highest values obtained for Serum transaminase studies.

CORRELATION OF LIVER FUNCTION TESTS TO SEVERITY OF DISEASE

Laboratory investigations

These have been tabulated in tables 8, 9, 10, & 11.

The majority of the patients had a total white count which was within the normal range for Malaysians and Indonesians (5,000 - 13,000/cumm). One child showed on peripheral smear, irregularly

contracted and fragmented cells, (anisopoikilocytosis). This with the presence of low platelet count of below 17,000/cumm and the clinical features of persistent fresh bleeding from various sites, made us suspect Disseminated Intravascular Coagulation Defect, and I.V. Heparin was given to this child. The platelet count was found to be the most useful investigation. From table 9, it can be seen that only 1 out of 11 cases belonging to grade III and in shock, had a normal platelet count of 100,000 - 200,000 whereas 6 cases out of 11 in Grade III had a very low platelet count of below 50,000/cumm. In slide 10, we observed that the cases showing evidence of hepato-cellular damage had a bad prognosis.

We did not find the estimation of serum amylase to be a very useful index in the few cases that were investigated.

Management of Patients in the Ward

When a patient of suspected Haemorrhagic Fever was admitted into the ward, the patient was first graded according to the severity of the disease.

Urgent investigations like TWDC, B.T.C.T. Platelet count were done. Blood for FBP and for viral studies were collected on admission in as many cases as possible.

1. Grade I, B.P. recorded every two hours to detect shock.

If platelet count was very low, (i.e. below 50,000/cumm.) we considered it as a sign of impending shock, and then the patient was given plasma at 30ml/kgm. The I.V. drip was maintained for about 24 hours using 1/5 D/S at slow rate.

2. Grade II & III. I.V. drip was started as soon as the patient was admitted. 1/5 D/S was used to start the drip. Fresh blood was only given in a few cases where the Hb was low.

3. I.V. Heparin given to one patient.

This child came in with large ecchymotic patches mainly on the abdomen and back, and was in coma III on admission. Meningococcal septicaemia was done. Blood started oozing from the lumbar puncture sites.

Later DIVC was suspected due to the following reasons.

1. Bleeding continuously from LP site.
2. Big ecchymotic patches all over the body.

A few of them later ulcerated.

3. Fresh bleeding from the mouth and nostrils.
4. Platelets count 17,000/cumm.
5. Prothrombin index below 70%.
6. Irregularly contracted and fragmented red cells. Presence of amispokilocytosis.

I.V. Heparin was given as a desperate measure at the rate of 100 units/kg/4 hourly. The patient made a remarkable recovery, I.V. drip was stopped when the platelet count came up to 31,000/cumm. Later a blood transfusion was given as Hb was low.

5. Pleural tapping.

Done on one patient in Grade III.

This child came in coma III and had several episodes of convulsions. Evidence of massive pleural effusion both clinically and radiologically.

Results (R) side 200cc) straw coloured fluid
(L) side 180cc)

Fluid — Protein 4 gm%

This child also made a remarkable recovery.

Lungs 2 cases had massive pleural effusion

Stomach Evidence of bleeding in Stomach in all 3 cases

Large intestine

1 case haemorrhage from caecum to rectum.

Liver all enlarged.

Brain 1 case petechial haemorrhages on the surface of the brain

Section No evidence of internal bleeding.

Histological picture was nonspecific suggestive of virus infection with evidence of internal bleeding in the lungs, spleen and kidney, which could be brought about by haemorrhagic fever.

Conclusion

The clinical features, diagnosis, management, and treatment of 45 positive cases are discussed. The majority of the cases were between the ages of 6 & 7 years. This age distribution was similar to that in the epidemics which occurred in Penang in 1962, Thailand in 1961 and 1969, and in Singapore in 1965. In the Singapore epidemic in 1961 young adults were mainly affected. In the clinical features, fever was present in all the cases, but was of a low grade type. Bleeding tendency was seen in 30 cases a positive Hess test was elicited in 22 cases. However we found that this was not a reliable sign in the presence of shock, as it was elicited only in 2 cases belonging to Grade III. Skin rashes (27) hepatomegaly (25) abdominal pain (21) were other common features. Shock was found in 11 cases, and its presence had a very bad prognostic sign. Convulsion occurred in 3 cases, 2 of whom died. Massive pleural effusion was seen in one case. Isolated facial palsy was an unusual finding in one case.

In the laboratory data we found the platelet count a very useful index in grading the severity and management of the cases. A low platelet count at the onset was taken as a danger signal and a level of below 60,000/cumm was an indication for plasma infusion. In the management of these cases, we found that plasma infusion was better than whole blood in combating shock. The use of I.V. Heparin in one case where disseminated intravascular coagulation defect was suspected resulted in a remarkable alteration of the bleeding tendency. It is recommended¹ that this feature should be looked for in the ve. ill cases. Pleural tapping is recommended if there is evidence of massive effusion and respiratory distress.

Table 7

Normal	5,000 - 10,000	-	20 cases
	10,000	-	11 cases
	5,000	-	14 cases
Lymphocytosis	40%	-	33 cases
Polymorphonuclear leukocytosis	60%	-	12 cases
Atypical Mononuclear cells		-	18 cases
1 case where heparin given		-	17,000 - low platelets; irregularly contracted cell and fragmented cells.

Mortality

One child Pang Saw Mooi was admitted on the 7th day of illness with a mild upper respiratory tract infection; on the 9th day in the afternoon, coughed up about 5 ml of fresh blood; about half an hour later she suddenly went into irreversible shock and died. Hence we found that shock could develop late in the disease.

Post mortem was done in 3 cases.

Naked eye appearance

Significant findings

**COMPARATIVE STUDY OF CLINICAL FEATURES
OF CASES SEEN IN PENANG, SINGAPORE, THAILAND & KUALA LUMPUR**

Clinical features	Singapore 1961	Thailand 1961 & 1969	Penang 1962	Singapore 1965	Kuala Lumpur 1973
Onset	Abrupt	Abrupt	Abrupt	Abrupt	Abrupt
Fever	100%	100%	100%	100%	100%
Nausea and Vomiting	60%	70%	83%	49%	49%
Abdominal Pain	Rare	23%	39%	26%	47%
Respiratory Symptoms	?	40%	7%		3%
Hepatomegally	Nil	4%	63.4%	6%	5%
Splenomegally	4%	Most cases	4%	3%	3%
Circulatory Failure	Absent	Present	Present	Present	Present
Thrombocyto-paenia	usual	usual	usual	usual	usual
Leucopenia	usual	uncommon	uncommon	-	usual
+ ve Hess test	usual	usual	common	-	common
Mortality	Nil	1961 1969 2% Nil	12%	30%	1%
Age Distribution	Young adult	children	children	children	children

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- 3) Doctors and Staff of Paediatric Unit, General Hospital, Kuala Lumpur.

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