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THE CLINICAL, SEROLOGICAL AND VIROLOGICAL ASPECTS OF DENGUE FEVER: A COMPARATIVE STUDY**

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Abstract

Objectives: **To describe the clinical, serological, and virological aspects of confirmed dengue infections among hospitalized patients.**

Design: **Prospective descriptive.**

Setting: **Pediatric ward, SLMC**

Subjects: **Previously healthy children admitted at SLMC between 2-17 years old, with fever of at least 37.8°C and above, fever of less than five days and no apparent cause of fever.**

Method: **Children meeting the criteria were examined by a pediatrician for eligibility. Informed consent obtained. Subjects and their parents were interviewed by the dengue team to take patient's medical history, perform physical examination and collect blood specimens for Day 1, 3, 4 and 7. $Sp0_2$ was measured & chest x-ray taken on Day3 irrespective of the lung findings. PCR and IgM ELISA were utilized to detect presence of dengue antibody and sereotype.**

Statistical Analysis: **ANOVA test and chi-square with correction factor.**

Results: **Total of 63 cases of clinically suspected dengue were reported and 30 were diagnosed dengue by virologic or serologic testing. All showed positive IgM ELISA but only 5 showed positive RT-PCR. No age nor sex predisposition noted but with seasonal pattern. Overall clinical findings were similar to previous studies. Out of 30 cases, 18 fulfilled all 4 requirement of the WHO Criteria. Most of the confirmed cases were diagnosed as classic DF and only one case was diagnosed as DHF IV who eventually developed shock and succumbed.**

Conclusion: **Clinically, DF still has similar presentation with flushing, abdominal pain and (+) tourniquet test as the most common symptoms. 60% were diagnosed DF and 40% DHF II. Only one developed shock. Progression to severe dengue infection was prevented by early diagnosis of clinicians. All showed (+) IgM ELISA and 5 showed (+) RT-PCR for serotyping.**

INTRODUCTION

Before Ebola, before Marburg, there was Dengue[1]. In the last twenty-five years, beginning in Southeast Asia, the dengue virus has begun to manifest itself as a more serious and often fatal disease among children and to a lesser extent in adults[2].

Benjamin Rush in Philadelphia first described Dengue Fever (DF) in 1780 as "breakbone fever". It was called "dengue" after an epidemic in Cuba in 1828. In 1927-1928, epidemic in Greece estimated 90% of the populace of Athens contracted dengue fever. In the Philippines however, Dengue Hemorrhagic Fever (DHF) was widely known in the 1954 outbreak where it was called as the Philippine Hemorrhagic Fever. This then became endemic and epidemic in many areas of Tropical Asia[3].

Dengue Fever and Dengue Hemorrhagic Fever is caused by the dengue viruses, which belong to the genus *Flavivirus*, family Flaviviridae. There are four antigenically related but distinct, dengue virus serotypes (DEN-1, DEN-2, DEN-3 and DEN-4), all of which can cause DF/DHF. All four serotypes however, have similar natural histories, including humans as the primary vertebrate host and *Aedes* mosquitoes of the subgenus *Stegomyia* as the primary mosquito vectors[4].

To clinically distinguish, DF is characterized by the onset of high fever, headache, severe myalgia, nausea, vomiting and a transient macular rash appearing 3 to 4 days after the onset of fever. The rash begins on the trunk with subsequent involvement of the extremities and face. DHF on the other hand, is a more pronounced form of dengue fever, characterized by severe thrombocytopenia, hemoconcentration and hemorrhagic manifestations[5]. Four severity grades of the illness are seen: Grade I (fever and constitutional symptoms), Grade II (grade I plus spontaneous bleeding of skin, gums and GI tract), Grade III (grade II plus agitation and circulatory failure), and Grade IV (profound shock)[6]. Therefore, patients with classic dengue fever should be monitored closely in the event that they develop this severe complication of dengue infection.

Today, dengue fever is currently one of the leading causes of hospitalization and death among children in several Southeast Asian countries. It is now considered the most widespread viral infection

Keywords: dengue fever, Dengue IgM Elisa, Dengue PCR

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transmitted in man by insects, whether measured in terms of the number of human infections or the number of deaths[7].

The present clinical pattern of dengue infection in the Americas is progressing in the same manner in which it evolved in Southeast Asia in the 1960's (JAMA 1988). In the initial epidemics, infections were of the classsical type that can be mistaken for influenza. Later outbreaks included cases of DHF or Dengue Shock Syndrome (DSS) which may be fatal in young children. Subsequent epidemics have become progressively larger, producing more cases of DHF or DSS and more fatalities (Gubler, 1992)[4]. Symptoms of these serious complications of dengue viral infection include rapid deterioration, physical collapse and sometimes death[1].

In the Philippines, observation of the illness among Filipino children was first reported in 1954 when 21 cases were described with a clinical syndrome similar to epidemic hemorrhagic fever in Korea. Two years later, in another report, some authors termed the disease Philippine Hemorrhagic Fever that was described in greater detail in clinical picture of 85 cases. In both papers, diagnosis was based on the clinical course of the illness and characteristic laboratory findings[8].

Some significant laboratory changes occur on patients with DHF, and understanding this is critical diagnosis and treatment[4]. Therefore, successful viral isolation and correlation between the clinical manifestations and the infecting serotype, can be a good tool for the clinician for a better understanding and management of dengue infection.

Thus, this study aims; 1) to describe the clinical, serological and virological aspects of confirmed dengue infections among hospitalized patients in St. Luke's Medical Center; 2) to determine the clinical manifestations in correlation to the severity of dengue infection and; 3) to compare the clinical pattern of the dengue virus infection then and now, specifically in relation to age and sex predominance, seasonal occurrence, and clinical presentation.

METHODOLOGY

I. Study Design

This is a pilot study, a part of an on-going study on Dengue in collaboration with the Research and Biotechnology Division (RBD) of St. Luke's Medical Center (SLMC) and Nagasaki University, Japan.

This study utilizes a prospective descriptive design.

II. Statistical Analysis

Analysis was done using ANOVA test for comparison of quantitative data and chi-square with correction factor for qualitative data. Multiple comparison using Bonferroni Procedure for quantitative data was likewise applied. A *p value* of less than 0.05 was considered statistically significant.

III. Definition

Patients with virological or serological (or both) diagnosis of acute dengue infection was assigned a final clinical diagnosis on the basis of clinical and laboratory data. The clinical diagnosis of DHF was determined following the WHO clinical definition (Annex A).

Annex A
Clinical Grading of DHF by WHO Criteria

	Hemocon-centration	Spontaneous bleeding	Hypotension	Shock
DHF I	+	0	0	0
DHF II	+	+	0	0
DHF III	+	+/-	+	0
DHF IV	+	+/-	+	+

On the basis of presence of plasma leakage and thrombocytopenia (less than 100,000/mm^3) The evidence of plasma leakage will include a peak hematocrit value>20% above the value of the convalescent specimen (study day 7), a pleural effusion demonstrated on chest radiograph or detection of ascites on physical examination. Case of DHF was graded from I to IV according to WHO criteria. Any subject with acute dengue infection who did not meet the criteria for DHF was considered DF.

IV. Study Population

Approximately 63 previously healthy children admitted at St. Luke's Medical Center (SLMC), Quezon City between January 1999 and August 1999 were eligible for entry into this study since they met the following criteria:

A. Age 2-17 years old
B. Fever of less than 5 days
C. Temperature of at least 37.8°C
D. No apparent cause of fever

Children meeting these criteria were examined by a pediatrician for eligibility. To be excluded were children who had fever for more than 5 days and with apparent focus of infection. Informed consent was obtained from parents of qualified patients.

The protocol was approved by the Institutional and Ethical Review Boards of St. Luke's Medical Center (SLMC) before the start of the trial.

V. Study Protocol

At the time of enrollment, the subjects and their parents were interviewed by the investigating pediatric resident together with the research nurse to take the patient's medical history, perform physical examination and collect blood specimens (Study Day 1). A tourniquet test was performed by inflating a blood pressure cuff on upper arm and midway between the systolic and diastolic blood pressure for five (5) minutes and examine a 2.5 cm^2 area using a standard template. Vital signs including blood pressure were obtained by the ward nurses at least 4-6 hours depending on the need. Every enrolled patient was clinically assessed daily by the investigators. SpO2 was also measured by a pulse oxymeter and a chest radiograph (PA or AP view) taken on the third day irrespective of the lung findings. All patients were admitted to the hospital ward for observation under the care of the Attending Medical Doctor (AMD) and residents with experience in the care of dengue patients. The clinical and laboratory data were recorded by the investigating pediatric resident and / or research nurse on the Case Record Form.

VI. Virological and Serogical Diagnosis

Serum samples were tested using Polymerase Chain Reaction (PCR) to detect for flavivirus and using Enzyme-linked Immunosorbent Assay (ELISA) to detect for IgM antibody to dengue viruses. The standard protocols used in the Research and Biotechnology Division, SLMC were followed.

VII. Study Design for Laboratory Examinations

A. *Blood drawing at Study Day 1 (Acute Phase)*
   1 ml EDTA blood for hemogram
   3 ml of plain blood
   0.15 ml serum for PCR
   0.15 ml serum for IgM ELISA

B. *Blood drawing at Study Day 3*
   3 ml of plain blood

C. *Blood drawing at Sudy Day 4*
   3 ml of plain blood
   0.15 ml serum for IgM ELISA

D. *Blood drawing at Study Day 7*
   3 ml of plain blood
   0.15 ml serum for IgM ELISA

E. *Chest Radiograph*
   This is requested on Day 3 irrespective of SpO_2 results. This is taken in PA or AP view only. If abnormal findings are present, lateral decubitus view is necessary.

F. *Hematological Examinations in cases of DHF (Clinically)*
   Bleeding time, Prothrombin time, fibrinogen and FDP will be done at Study Day 3 for all enrolled patients found to be clinically manisfesting DHF.

G. *Arterial Blood Gas (ABG)*
   ABG will be performed in cases of low SpO_2 (<90%). ABG will be followed depending on the doctor's descretion, if SpO_2 is going down.

RESULTS

From January 1 through August 31, 1999, a total of 63 cases of suspected dengue (i.e. disease in persons for whom a diagnostic serum sample was submitted) were reported (Figure 1). Out of the 63 clinically suspected cases, 30 (48%) were diagnosed as dengue (DF/DHF) by virologic or serologic testing. 23 (36%)

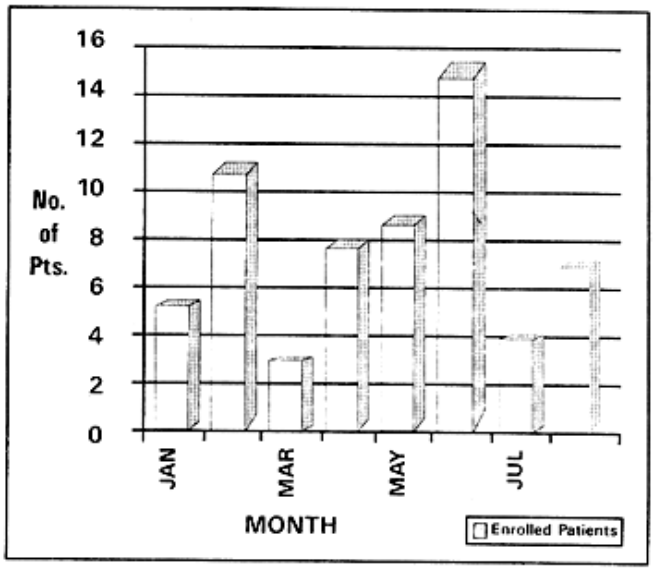

Figure 1. Dengue Census from January 1999 to August 1999

were negative serologically and 10 (16%) were indeterrminate (i.e., testing was not complete or acute phase serum was negative and no convalescent phase sample was submitted).

Of these 30 confirmed cases, 18 (60%) were given the final diagnosis of dengue fever and 12 (40%) were diagnosed dengue hemorrhagic fever both clinically and serologically. Of the DHF patients, 9 (30%) were classified as DHF II, 2 (7%) were DHF III only 1 (3%) was DHF IV as shown in Table 1.

Table 1. **Final Diagnosis of 30 Confirmed Dengue Cases**

Final Diagnosis	No. of Cases	
Dengue Fever		18 (60%)
DHF		
I	0	
II	9	12 (40%)
III	2	
IV	1	
Total		30 (100%)

The remaining 33 (52%) had a final diagnosis as follows: 9 (27%) as acute respiratory infections (ARI), 19 (58%) systemic viral infections (SVI), and 5 (15%) other non-dengue febrile illnesses.

Among the 30 confirmed cases, 17 (57%) were males and 13 (43%) were females with a male to female ratio of 1.3:1 This shows that just like in previous studies, ther is still no sex predelection in dengue infection. Both males and females were equally affected (FIGURE 2).

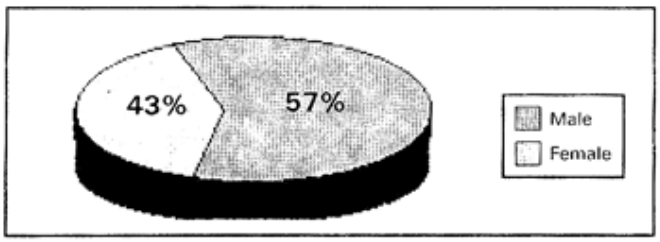

***FIGURE 2.* Sex predominance**

Likewise, in relation to the final diagnosis, of the 18 DF patients, 7 were males and 11 were females. And of the 12 DHF patients, 10 were males and 2 were females. It may look remarkable in DHF cases, but when computed was not statistically significant. (TABLE 2).

Table 2. **Sex Distribution According to Final Diagnosis**

	DF	DHF	P value
Male	7 (39%)	10 (83%)	>0.05
Female	11 (61%)	2 (17%)	(NS)

The ages ranged from 2 to 17 years old with a median age of 8.5 years. Majority of them belonged to the age bracket of 11-17 years old (TABLE 3 & FIGURE 3).

TABLE 3. **Age predominance.**

AGE IN YEARS	FREQUENCY	PERCENTAGE
2-5	5	16.7%
6-10	12	40.0%
11-17	13	43.3%
Mean (+/-SD) = 9.57 +/- 3.97		
Mode = 8		
Median = 8.5		

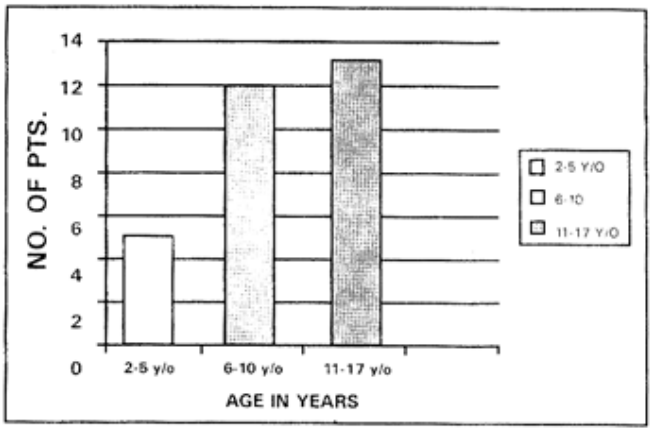

***FIGURE 3:* Age Predominance**

Of the 30 confirmed cases, all showed a positive IgM ELISA test which detects dengue virus in the blood. And only 5 (17%) showed positive in RT-PCR test for determining the serotype of the dengue virus in the blood (TABLE 4).

TABLE 4. **IgM ELISA and RT-PCR in 30 confirmed cases.**

Final Diagnosis	RT-PCR	IgM ELISA
Dengue fever	3(10%)	18% (60%)
DHF I II III IV	2(7%)	12 (40%)
Total	5 (17%)	30 (100%)

Specifically, these serotypes includes DEN 1, DEN 2, DEN 3. Most of them, 3 (10%) showed positive for DEN 1. The remaining 2 were positive for DEN 2 and DEN 3 (Table 5).

TABLE 5: **Dengue serotypes**

Serotypes	Frequency	Percentage
DEN1	3	10%
DEN 2	1	3.3%
DEN 3	1	3.3%
Total	5	16.6%

Of the 3 patients who showed positive for DEN 1, 2 had a final diagnosis of DHF III. The patient who showed positive for DEN 2 had a final diagnosis of DHF III and the one with DEN 3 serotype was diagnosed as DHF II (TABLE 6).

TABLE 6: **Final diagnosis according to Dengue Virus (serotype)**

Serotype	DF	DHFI	DHF II	DHF III	DHF IV	P VALUE
DEN 1	2			1		>0.05
DEN 2				1		NS
DEN 3			1			NS

Of the 30 cases who showed positive for IgM ELISA, 18 cases (60%) fulfilled all 4 requirements of the WHO criteria. The remaining 12 cases (40%) satisfied only 2 or 3 of the criteria (TABLES 7 & 8).

TABLE 7. **WHO Criteria:**

WHO Criteria	No. of Patients (n=30)	Percentage
Fever		
(+)	30	100%
(-)	0	0
Tourniquet test or Spontaneus bleeding		
(+)	26	87%
(-)	4	13%
Hemoconcentration		
(+)	30	100%
(-)	0	0
Thrombocytopenia		
(+)	25	83%
(-)	5	17%

TABLE 8: **WHO scoring.**

WHO Score	No of Patients (n=30)	Percentage
1	0	0
2	8	27%
3	4	13%
4	18	60%
Total	30	100%

Table 9 and Figure 4 show the number of days of fever when patient was admitted in the hospital. From day 1 to day 5 of fever, most patients, 13 (43.3%) were admitted already on Day 4 of fever: 7 (23.3%) were admitted either on Day 3 or Day 5 of fever. Only 2 (6.7%) were admitted at the onset of fever.

TABLE 9: **Days of fever upon admission**

Days of fever	Frequency	Percentage
1	2	6.7%
2	1	3.3%
3	7	23.3%
4	13	43.3%
5	7	23.3%
(Mean +/- SD) = 3.53 +/- 1.11		
Mode = 3		
Median = 3		

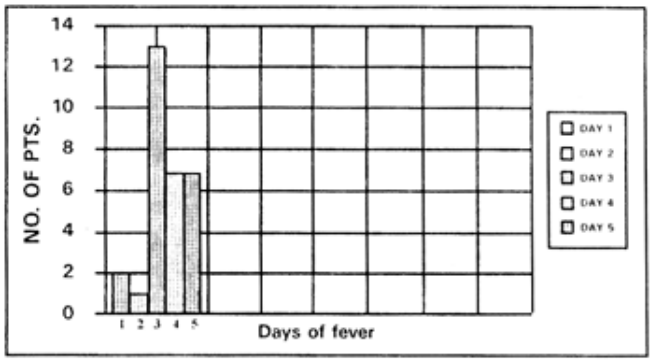

FIGURE 4: **Days of fever upon admission.**

All 30 confirmed cases were admitted with a chief complaint of fever. Flushing was seen in 26 case (87%), abdominal pain were seen in 15 cases (50%) and vomiting in 14 cases (47%). Table 10 shows the rest of the non-specific signs and symptoms presented by dengue patients.

TABLE 10: **Non-specific signs and symptoms**

Findings	No. of Patients	Percentage
Fever	30	100%
Flushing	26	87%
Loss of appetite	16	53%
Abdominal Pain	15	50%
Vomiting	14	47%
Pleural effusion	3	10%
Restlessness	3	10%
Headache	3	10%
Cough	3	10%
Hepatomegaly	2	7%
Diarrhea	2	7%
Colds	1	3%

For the hemorrhagic signs and symptoms, most patients showed positive for tourniquet test and palatal petechiae in 26 cases (87%). Other forms of spontaneous bleeding noted were epistaxis in 10 cases (33%), Herman's rash in 5 cases (17%) and gum bleeding in 2 cases (7%) as shown in Table 11.

TABLE 11: **Hemorrhagic signs and symptoms.**

Findings	No. of Patients	Percentage
Palatal petechiae	26	87%
(+) Tourniquet test	26	87%
Epistaxis	10	33%
Herman's rash	8	27%
Gum bleeding	2	7%
GI bleeding	2	7%
Shock	1	3%
Hemoptysis	0	0
Hematuria	0	0

In relation to the Dengue Classification, all 18 patients diagnosed as DF presented with fever, out of the 18 cases, 15 (83%) presented with skin flushing, positive tourniquet test and palatal petechiae. For DHF II patients, all the 9 cases (100%) also presented with fever. Out of these, 8 cases (89%) presented with skin flushing, positive tourniquet and palatal petechiae and epistaxis, and 7 cases (78%) with abdominal pain. For DHF III patients, all 2 cases (100%) had fever, signs of spontaneous bleeding, hypotension. We had only 1 diagnosed DHF IV case who presented with fever, signs of spontaneous bleeding, hypotension and who eventually developed dengue shock syndrome (TABLE 12).

TABLE 12: **Clinical Manifestations of Confirmed Dengue patients in Relation to the Dengue Classification**

Clinical Manifestation	Dengue Classification					Percentage
	DF n=18	DHF I n=0	DHF II n=9	DHF III n=2	DHF IV n=1	n=30
Subjective:						
Fever	18		9	2	1	30 (100%)
Flushing	15		8	2	1	26 (87%)
Loss of appetite	9		6	1		16 (53%)
Abdominal pain	5		7	2	1	15 (50%)
Vomiting	10		4			14 (47%)
Epistaxis			8	1	1	10 (33%)
Cough & colds	4					4 (13%)
Restlessness	3					3 (10%)
Headache	3					3 (10%)
Diarrhea	2					2 (7%)
Hematemesis/ Melena				1	1	2(7%)
Gum bleeding				1	1	2 (7%)
Objective:						
(+)Tourniquet test	15		8	2	1	26(87%)
Palatal petechiae	15		8	2	1	26 (87%)
Herman's rash			5	2	1	8(27%)
Pleural effusion				2	1	3(10%)
Hypotension				1	1	2(7%)
Hepatomegaly				2	1	3 (10%)
Shock					1	1(3%)

As for the laboratory findings, it is noteworthy to mention that all diagnosed DF patients had hemoconcentration, 13 cases (72%) out of 18, had thrombocytopenia while 5 cases (28%) had low platelet count. For DHF II patients, all 9 cases (100%) showed thrombocytopenia and hemoconcentration, with 5 cases (56%) of prolonged PTT. For DHF III patients, all presented with thrombocytopenia, hemoconcentration, and prolonged PT and PTT. Our only DHF IV case showed similar laboratory findings but the bleeding was also prolonged thus the patient went into shock (TABLE 13).

TABLE 13: **Laboratory findings of the confirmed Dengue patients in relation to the Dengue Classification**

Laboratory Findings	DF n=18	DHF I n=0	DHF II n=9	DHF III n=2	DHF IV n=1
Low normal platelet count	5 (28%)				
Thrombocytopenia	13 (72%)		9 (100%)	2 (100%)	1 (100%)
Hemoconcentration	18 (100%)		9 (100%)	2 (100%)	1 (100%)
Prolonged bleeding time					1 (100%)
Prolonged PT				2 (100%)	1 (100%)
Prolonged PTT			5 (56%)	2 (100%)	1 (100%)

DISCUSSION

Dengue causes more illness and death than any other arboviral infection: there are at least 20 million infections in the world each year and several hundred thousand cases of severe, life-threatening syndrome known as Dengue Hemorrhagic Fever / Dengue Shock syndrome[9].

This worldwide incidence of dengue has increased dramatically in the period following Worl War II, due to expanding urban human populations and a coincident increase in *Aedes aegypti* density, as well as the advent of air travel and rapid movement of viremic persons[10]. Most dengue virus infections in children have minimal or no symptoms and cannot be easily distinguished clinically from other viral infections[11]. Because clinical findings vary and there are many possible causative agents, the term "dengue-like diseases" should be used until a specific diagnosis is established[12].

Except for the painful symptoms, which have led to the name "breakbone fever", classic dengue fever is relatively mild disease and is rarely fatal[13]. Thus, early studies of dengue in Southeast Asia understandably focused on DHF / DSS, the most dramatic manifestations of dengue[14].

This study conducted in a private hospital, describes the clinical, serological and virological aspects of the confirmed dengue infection among hospitalized patients. From a total of 63 clinically suspected dengue cases, 30 were diagnosed as dengue by virologic or serologic testing.

From January to August 1999, it was noted that the peak of dengue cases during this time was on the month of June. In a local study by Baltazar et al, it stated that, while dengue infections occured throughout the year, it has the tendency to increase in July and February[15]. This may account for the fact that dengue has a seasonal pattern and occurs more frequently during the rainy season[16]. Likewise, according to Halstead, Dengue outbreaks in the tropic, generally coincide with the monsoon season as there is evidence that biting rates increase during higher humidity[17].

Furthermore, it was found out that just like in previous local studies, the one done by Manoloto et al[18] and Tapusi et al[19], no sex predisposition was noted. Both males and females were equally affected with male to female ratio of 1.3:1 as in fig. 2.

As to age, majority of the subjects belonged to 11-17 year old with a median age of 8.5 years (Figure 4). In the study of Cristobal et al[20] in 1991, the incidence was highest in 5-9 years old. This further shows that all children from all ages and in both sex were affected by the dengue infection.

As dengue is the most important mosquito-borne disease in the world in terms of morbidity and mortality, a rapid and reliable test is necessary[21]. For the control and prevention of DF, it is important to rapidly detect and type the virus in clinical samples of mosquitoes[22].This can be done by using the Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) which determines the serotype of the dengue virus. On the other hand, IgM antibody-capture Enzyme-Linked Immunosorbent Assay (IgM-capture ELISA) is said to be the most useful serologic procedure available for determining recent infections by dengue virus[4]. In this study, both tests were utilized. It showed that all of the 30 confirmed dengue cases were positve for IgM ELISA but only 5 of them showed positive in RT-PCR determination.

Although classic dengue fever is characterized by an incubation period of 3-5 days with fever usually lasting 2-7 days[23], in this study it was noted that most patients were admitted already on day 4 of fever, at which time the dengue virus is rapidly diminishing in the blood. According to Vorndam and Kuno dengue virus replicates and reaches peak titers in the blood before the patient becomes sick enough to present to a physician. The circulating virus remains readily

detectable in the blood up to 5 days after onset of symptoms. For this reasons, it is imperative that an acute phase serum sample be collected as soon as possible after onset of symptoms[4]. This is probably one of the limitations of the study.

As to the clinical manifestations, this study showed similar findings with the local studies mentioned above (Tupasi et al and Manoloto et al) and the study of Inciong et al[24]. In all studies, the most frequent non-specific findings were flushing, anorexia, abdominal pain and vomiting. While the most common hemorrhagic manifestations were: positive tourniquet test, palatal petechiae and epistaxis. Laboratory-wise, hemoconcentration and thrombocytopenia were the most consistent observations.

Likewise in this study, the WHO Criteria for the diagnosis of DF/DHF was used. These criteria require the presence of fever with a temperature more than 38°C lasting for 2-7 days, hemorrhagic manifestations such as nose bleeding and gum bleeding, hemoconcentration and thrombocytopenia for a case to be labeled DHF[25]. Results show that 18 cases fulfilled all 4 requirements of the WHO Criteria, while the remaining 12 cases satisfied only 2 or 3 of the criteria. These findings were comparable to the local studies previously mentioned.

However, unlike in the above-mentioned local studies, most of the confirmed cases were diagnosed as a classic DF in 18 cases followed by DHF in 9 cases. Only 1 case was diagnosed as DHF IV that eventually led to dengue shock syndrome. This was our only mortality case that an eight year old male from Rizal who was admitted already during the late stage of dengue. He presented with 3 days fever associated with flushing, restlessness, vomiting with epistaxis and melena; who on physical examination was tachypneic with positive tourniquet test and palatal petechiae with hypotension (80/60 mmHg), narrowed pulse pressure and weak thready pulses. On auscultation, a decreased breath sound was noted more on the right. Chest x-ray was done and showed presence of pleural effusion, bilateral. Thrombocytopenia was noted as low as 15,000 and FFP was transfused. He developed signs of respiratory distress and was eventualy intubated. His condition however deteriorated fast and he subsequently succumbed on the 4th hospital day. Discharge diagnosis was DHF IV, dengue shock syndrome.

Systematically, in DSS, the abnormal vascular regulation is manifested by mild hypotension in the early stage of the disease and by shock in more severe and advanced infections. Vascular damage may be evident as capillary leakage in non-dependent cases[26]. According to the study of Rigau-Perez, the case fatality rate in patients with DSS can be high as 44%. Thus, for decades now, two distinct hypotheses to explain the mechanism of DHF have been debated - secondary infection or viral virulence. However, a combination of both now seems to be the plausible explanation[27].

Prospects for reversing the trend of increased epidemic DF/DHF are promising. New dengue virus strains and serotypes will likely continue to be introduced in many areas where *Aedes aegypti* occurs, thus resulting in increased frequency of epidemic activity and incidence of DHF. It is therefore imperative to support research on new mosquito control technology and on prevention strategies, including dengue vaccines, and for all countries in endemic areas to develop new emergency control strategies measures for epidemic DF/DHF.

CONLUSION

Several studies have already been conducted to elucidate dengue fever. Much has already been said about it. But the fact remains that dengue fever / dengue hemorrhagic fever is still one of the most dreaded infection of all times.

Previous studies up to the present shows that clinicians are adept and reliable enough to diagnose dengue fever clinically, based on history and clinical manifestations. And people from all walks of life may be aware of this infection, but not enough to significantly control its spread. Environmental hygiene and the use of repellant are only some of the ways to help control its emergence, but once infection sets in, early check up with the clinician is vital to the outcome of the patient.

In this study, it was noted that ***clinically***, dengue fever still has similar presentations: with flushing, abdominal pain, vomiting, (+) tourniquet test and palatal petechiae as the most common presenting signs and symptoms. Laboratory wise, hemoconcentration and thrombocytopenia are comparatively common. More than half of the confirmed cases or 60% were diagnosed clinically as DF and only 40% were DHF II. Progression to a severe form of dengue infection was clearly prevented by early diagnosis. This can be further proven by the fact that mortality rate was only 3%. ***Serologically*** and ***virologically*** however, it was noted that although all showed positive for IgM ELISA, only 5 or 17% showed positive for RT-PCR for serotyping. This signifies the importance of early

consult at the first onset of fever in order for the clinician to be able to detect the dengue virus as it reaches its peak titers in the blood.

Currently, prevention of dengue infection depends on controlling its mosquito vector. However, everyone knows that development of a vaccine will offer greater hope in the long term.

RECOMMENDATIONS

As this infection is endemic in this country, and as it continuously occurs in varying proportions, a more rigid investigation from all aspects is indicated.

Emphasis on vector control should once again be highlighted.

Rigorous mass health education should be taken, not only regarding proper disposal of wastes / empty cans or environmental hygeine in general, but emphasis on early consult at the first sign of fever should be done so that the dengue virus can be detected just as it reaches its peak titers in the blood. In this way, a better correlation between the dengue virus serotype and severity of infection can be possible.

Lastly, everyone's dream of vaccine production will hopefully become a reality.

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