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ORIGINAL ARTICLES

Editorial: Keep Calm, The New Editors are Here

Cecilia C. Maramba-Lazarte MD 2-3

ORIGINAL ARTICLES

Randomized Controlled Trial on the Effect of Coconut Oil, Vinegar Plus Cooking Coconut Oil Versus 1% Permethrin Shampoo in the Treatment of Pediculosis

Marian Moreno-Alsusua, MD 4-13

Predictors of Mortality among Pediatric Patients with Leptospirosis: A Multicenter Retrospective Study

Rosalia Belen F. Bonus, MD, Grace Devota Go, MD,
Joanne De Jesus, MD, Marxengel Asinas_Tan, MD,
Cecilia C. Maramba-Lazarte, MD 14-28

Cardiac Involvement in Kawasaki Disease Patients:

A Retrospective Study

Pilarica I. Caguiat, MD, Cherica A. Tee, MD, Leonila F. Dans, MD... 29-36

Clinical Profile and Outcomes in Acute Viral Encephalitis

Albert Roland Alcaraz, MD, Martha Lu-Bolanos, MD,
Ma. Liza Antoinette M. Gonzales, MD 37-46

The Use of Fluorescent Marking Technique as an Indicator Of Cleanliness and Disinfection in the Neonatal Intensive Care Unit

Expedito T. Yala, MD*; Cecilia C. Maramba-Lazarte, MD 47-55

Childhood Immunization Schedule 2017 57-60

Albert Roland Alcaraz, MD*
Martha Lu-Bolanos, MD*
Ma. Liza Antoinette M. Gonzales, MD*

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ORIGINAL ARTICLE

CLINICAL PROFILE AND OUTCOMES IN ACUTE VIRAL ENCEPHALITIS

ABSTRACT

Objective: This study aimed to determine the clinical profile and outcome of pediatric patients with acute viral encephalitis syndrome admitted at a single tertiary government hospital.

Methods: All pediatric patients admitted at the Philippine General Hospital from January 2011 to December 2014 and discharged with a final diagnosis of acute viral encephalitis were included. After demographic data, clinical manifestations, and laboratory findings were collected, the outcome was determined using the Modified Rankin Scale for children. The data were summarized using descriptive statistics. The median test was used to compare the outcomes while the chi-square test was used to analyze the comparison between study groups.

Results: Sixty-four patients diagnosed with acute viral encephalitis syndrome were included in the study. The highest number of cases was reported in ages 1- 4 years (32.81%) and among the male population (68.75%). The most common symptoms were seizure (46.87%), abnormal behavior (21.88%), and altered sensorium (20.31%). Forty-four patients had CSF viral studies done, and among them, the 11 (25%) were positive for Japanese encephalitis. The modified Rankin scale showed that 41 (64.08 %) subjects showed good outcomes, while 23 (35.23%) exhibited poor outcomes. There was no significant difference in the modified Rankin scale for Japanese encephalitis compared to the other etiologic agents of acute viral encephalitis (p value= 0.717).

Conclusion: In patients with acute viral encephalitis, the most common symptoms were seizures, abnormal behavior, and altered sensorium. Majority of the subjects did not show any significant symptoms and disability. No difference was seen in the clinical outcome of patients infected with Japanese encephalitis compared to other etiologic agents, but these results need to be verified by larger studies.

KEYWORDS:

Acute viral encephalitis, acute encephalitis syndrome, Japanese encephalitis, dengue encephalitis

INTRODUCTION

Acute encephalitis syndrome (AES) is an unusual manifestation of common viral infections and can lead to considerable morbidity and mortality. It commonly affects children and young adults. Several studies have reported an incidence of 2.5–to-8.8 per 100,000 persons per year; however, this may be underestimated particularly in developing countries where appropriate diagnostic tools are lacking.^{1,2} Viral meningoencephalitis is characterized as an acute inflammatory process involving the meninges and the brain tissue. The CSF is characterized by lymphocytosis and the absence of microorganisms on Gram stain and routine bacterial culture. In most instances, the infection is self-limited with good prognosis, although there could be substantial morbidity and mortality, depending on the etiologic agent.^{1,2}

Several studies across Asia have shown that Japanese encephalitis virus (JEV), dengue, and chikungunya are the most common etiologic agents in acute viral encephalitis. A study done by Beig showed that Enteroviruses were the most common isolates; although this was based solely on serologic studies and were not culture-confirmed.^{1,2} The diagnosis requires a strong clinical suspicion for sporadic and endemic cases which usually presents as fever, headache, vomiting, meningeal signs and altered sensorium.^{1,2} A study performed by Kakoti et.al. showed that most patients diagnosed with Japanese encephalitis presented with fever and altered sensorium, the majority of whom recovered but with significant neurologic sequelae^{1,2}. Suryawanshi et. al. showed that 6.9% of patients with encephalitis presented with altered sensorium and new onset seizures³. In the Philippines, a systematic review confirmed that Japanese encephalitis virus (JEV) is an important cause of encephalitis and present in all regions of the country⁴.

Acute encephalitis syndrome is associated with significant morbidity hence, timely and appropriate supportive care is the key to preventing neurologic sequelae. Additional data on the clinical profile and outcome of pediatric patients with acute viral encephalitis is important in order to initiate early supportive and preventive measures. This study aimed to determine the etiologic agents, describe the clinical profile and determine the outcome of pediatric patients admitted for acute encephalitis syndrome at the Philippine General Hospital from January 2011 to December 2014.

MATERIALS AND METHODOLOGY

Description of the Study Setting

The Philippine General Hospital is the national university hospital of the Philippines and the largest tertiary government hospital in the country. It is a state-owned hospital with a 1,500-bed capacity administered and operated by the University of the Philippines Manila. Being a tertiary referral center, it receives patient referrals from other institutions all over the archipelago.

Subjects

Inclusion Criteria

All pediatric patients aged 18 years and below who were admitted for acute encephalitis syndrome (AES) or who had a final diagnosis of acute viral encephalitis, viral encephalitis, or viral meningoencephalitis at the Philippine General Hospital from January 2011 to December 2014 were included in this study. The World Health Organization's (WHO) case definition for AES⁷ was adopted for this study, which was fever or recent history of fever with a change in mental status (including confusion, disorientation, coma, or inability to talk) and/or with new onset of seizures (excluding simple febrile seizures). Other early clinical findings include increased irritability,

somnolence or abnormal behavior greater than that seen with usual febrile illness were included. This study also included patients with CSF findings suggestive of viral meningitis (normal to elevated WBC count, the lymphocytic predominance of the differential count, normal to elevated protein and CSF/ Serum glucose ratio is normal) and was negative for bacterial culture or had no CSF specimens sent for viral studies.

Exclusion criteria

The study excluded pediatric patients with co-morbidities such as cerebral palsy, congenital heart diseases, and hematologic malignancies.

Data Collection

The logbook of patients and database of the Section of Pediatric Neurology, Department of Pediatrics was utilized to identify the study subjects. All pediatric patients suspected or confirmed to have acute viral encephalitis or acute encephalitis syndrome were referred to and were co-managed by the Section of Pediatric Neurology. Data on the patients' demography (ie, age, sex and residence address), including the signs and symptoms associated with the illness, and their outcome at the time of discharge were collected. Results of the CSF viral studies, including the method of testing (viral serology), were also recorded.

Clinical outcome at the time of discharge was determined using the modified Rankin scale originally introduced in 1957 by Dr. John Rankin from Stobhill Hospital in Glasgow, Scotland, United Kingdom that was commonly used to measure the degree of disability or dependence on the activities of daily living of people who suffered a stroke or other causes of neurological disability. It correlates directly with several physiological indicators including the size of lesion and type and provides a common language for all healthcare providers in

describing the degree of disability. A scale was also developed for children. Based on the scale, clinical outcome was assessed as follows:

- 0 -No symptoms at all;
- 1 - No significant disability despite symptoms in the clinical examination; age-appropriate behavior and further development;
- 2 - Slight disability; unable to carry out all previous activities, but same independence as other age- and sex-matched children (no reduction of levels on the gross motor function scale);
- 3 - Moderate disability; requiring some help, but able to walk without assistance; in younger patients adequate motor development despite mild functional impairment (reduction of one level on the gross motor function scale);
- 4 - Moderately severe disability; unable to walk without assistance; in younger patients reduction of at least 2 levels on the gross motor function scale, and unable to walk unassisted;
- 5 - Severe disability; bedridden, requiring constant nursing care and attention;
- 6 - Dead.

Data Analysis

Stata 12 (StataCorp., College Station Texas, USA) was used to analyze the data that have been tabulated using Microsoft Excel. The patient's characteristics, etiologic agents, and clinical outcomes were summarized using descriptive statistics and reported as frequencies and proportions. The clinical outcome of patients with JEV was compared to those with other etiologies (non-JEV) using the Mood's median test or a non-parametric test performed on the median of populations from which two or more samples drawn are assumed to be identical. Subsequently, the comparison between the two groups was analyzed using chi-square test. A p value of <0.05 was considered as statistically significant.

Ethical Considerations

This study was approved by the hospital ethics review board and respected patient confidentiality. The trial was conducted in accordance with the principles of the Declaration of Helsinki

RESULTS

A total of 75 patients admitted at the Philippine General Hospital from January 2011 to December 2014 were diagnosed to have acute viral encephalitis. The medical records of 64 patients (85%) were retrieved. The 1-4 years age group had the most number of patients presenting with signs and symptoms of acute encephalitis syndrome (Table 1); the youngest patient was 5 months old. There were more male patients than females, with the highest number of cases coming from Region IV. One patient came all the way from Northern Samar.

Table 2 shows the clinical profile of patients with acute viral meningoencephalitis, with the most common presenting symptom being a seizure (46.87%), followed by abnormal behavior (21.88%), and altered sensorium (20.31%). No other clinical symptoms were reported such as irritability, vomiting, diarrhea, Glasgow Coma Scale (GCS) less than 8 and signs of meningeal irritation.

Out of the 44 patients who submitted CSF specimens at the Research Institute of Tropical Medicine (RITM), 26 (59.1%) patients were confirmed to have viral encephalitis by CSF viral serological tests, while 18 (41%) patients had no viral pathogens identified. Results of the CSF viral serology showed the following positive results: JEV-specific IgM antibody (25%), dengue-specific IgM or dengue-specific-IgG antibody (20.5%), Herpes simplex virus-IgM and Herpes simplex virus- IgG antibody (13.6%) Eighteen (40.9%) of the 44 specimens had no viral pathogen identified but the clinical and CSF findings were consistent with viral etiology and were negative on bacterial culture. The CSF specimens were not sent for viral culture and

laboratory examinations for Chikungunya and other adenoviruses were not available at the time of the study.

Majority of the patients showed no significant symptoms (23.4%) and disability (21.9%) (Table 4). Of the 13 patients who had a severe disability (20.31%), 4 were positive for JEV, 1 was positive for dengue, and the remaining 8 patients were negative for the viral antibody titers tested. There were 3 patients who died, all of whom were diagnosed to have dengue: one case with probable dengue based on a positive dengue antibody titers, and 2 were diagnosed as suspected dengue based on clinical presentation. There were no deaths in the JEV group.

The comparison of outcomes in the 11 patients with JEV and 33 patients with other viral etiologies (Non-JEV) are shown in Figure 1. Although there were no mortalities in the JEV group, there were 4 patients who had scores higher than the median score of 2 which indicates moderately severe disability while most patients in the non-JEV group had an outcome of 1 which indicates no significant disability.

As seen in Table 5, the median for both groups was 2. For the 11 cases of Japanese encephalitis virus, 7 had outcome scores lower than or equal to the median, while 4 had scores higher than the median. In comparing the 33 non-JEV cases, 21 had scores lower than or equal to the median while 11 had scores higher than the median. The Mood's median test was used to determine the frequency of outcome scores that were lower or higher than the median. Although there were more patients who had scores higher than the median in the non-JEV group compared to the JEV group (11 versus 4, respectively), suggesting poorer outcomes in the non-JEV group, this was not shown to be statistically significant (chi-square test, p-value = 0.717).

Table 1. Demographic Data of Patients With Acute Viral Encephalitis

	Number	Percentage
Age (in years)		
<1	4	6.3%
1-4	21	32.8%
5-9	7	11.9%
10-14	18	28.1%
15-18	14	20.9%
Sex		
Male	44	68.8%
Female	20	31.3%
Location		
National Capital Region	19	29.7%
Las Pinas City	2	
Malabon City	2	
Manila	6	
Navotas City	1	
Paranaque City	3	
Pasay City	3	
Taguig City	1	
Valenzuela City	1	
Cordillera Administrative Region		
Kalinga	1	1.6%
Region 3	5	7.8%
Bulacan	3	
Nueva Ecija	1	
Zambales	1	
Region 4	37	57.8%
Batangas	3	
Cavite	17	
Laguna	12	
Oriental Mindoro	1	
Palawan	1	
Quezon	3	
Region 5	1	1.6%
Camarines Norte	1	
Region 8	1	1.6%
Northern Samar	1	
Total	64	100%

Table 2. Presenting Symptoms of Patients with Acute Viral Encephalitis Syndrome

Symptom	Total	Percentage
Seizure (generalized tonic clonic or partial)	30	46.9%
Abnormal behavior	14	21.9%
Altered sensorium	13	20.3%
Fever (temperature >37.8°C)	6	9.4%
Headache	1	1.6%
Total	64	100%

Table 3. Etiology of Patients With Acute Viral Encephalitis based on Serologic Tests*

Viral Pathogen	Number (N=44)	Percentage
Japanese encephalitis virus	11	25.0%
Dengue virus	9	20.5%
Herpes simplex virus (HSV type 1 and 2)	6	13.6%
No viral pathogen	18	40.9%
TOTAL	44	100%

* Results are based on CSF viral serologic tests: JEV-specific IgM antibody, dengue-specific IgM or IgG antibody, Herpes simplex virus-IgM or IgG antibody

Table 4. Clinical Outcome Of Patients With Acute Viral Encephalitis at Discharge Using the Modified Rankin Scale

Outcome (Modified Rankin Scale)	Total	Percentage
0 – No significant symptoms	15	23.4%
1 – No significant disability	14	21.9%
2 – Slight disability	10	15.6%
3 – Moderate disability	2	3.1%
4 – Moderately severe disability	6	9.4%
5 – Severe disability	13	20.3%
6 – Dead	3	6.3%
Total	64	100%

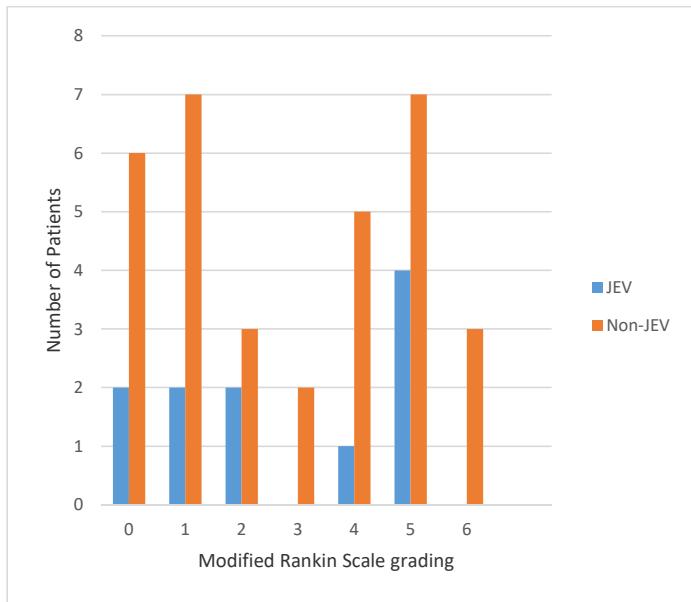


Figure 1. Comparison of Clinical outcomes using the Modified Rankin Scale in Patients with JEV and non-JEV (Dengue, Herpes simplex)

Table 5. Comparison of outcomes between the JEV group and the Non-JEV group

	JEV * (n=11)	Non- JEV** (n=33)	P value
Modified Rankin Scale Result			
Median	2	2	
Standard deviation	2.10	1.90	
Mood's Median test			
Outcome lower than the median (scores ≤ 2)	7	1	0.717
Outcome higher than the median (scores >2)	4	11	

* JEV- Japanese encephalitis virus

** non-JEV- dengue, herpes simplex virus,

DISCUSSION

In the Philippines, acute encephalitis syndrome is considered an important public health problem and is a reportable disease. Based on the Department of Health Philippine Integrated Disease Surveillance and Response (PIDSR)2014 annual report, there were a total of 226 suspected cases of acute encephalitis syndrome, the majority of whom were males(60.18%). The majority of cases came from Region XII in Mindanao, which is also the region with the highest number of mortalities. The highest number of

cases was reported during the 15th week of the year around May-June with an average of 15 cases seen. It is worth mentioning that the cases recorded in the National Capital Region decreased by as much as 9.8% compared to the PIDSR 2013 annual report.⁵ The Philippines' climate has an extended rainy season which served as an ideal breeding ground for the mosquito vectors and the main source of income of rural areas still is agricultural hence several animals can serve as adequate hosts as well. Majority of the patients diagnosed with acute encephalitis syndrome were mostly males possibly because they take a predominant role in the workforce and younger males tend to be more physically active hence posing an increased risk for the infection. The study of Lopez et. Al showed that viral encephalitis, including Japanese encephalitis, was associated with a high burden of disease and nationwide distribution. The first outbreak was recorded in 1982 from Nueva Ecija which was located in Region III. Several cases were also recorded from Cotabato and Pangasinan but the laboratory tests were not available. Majority of the cases were noted in Region V and Region VI.⁶ However, this study showed that majority of the cases were seen in Region IV, with the majority of patients coming from Cavite and Laguna probably due to the proximity of these provinces to the Philippine General Hospital, a tertiary government referral center.

This study was able to describe the clinical profile and outcome of acute viral encephalitis among patients admitted at PGH. Similar to PIDSR Annual report 2014, the majority of the cases were males and belonged to two groups: the 1-4 and 5-14 age group respectively.⁵ In this study, because of differences in groupings, the majority of the cases came from the 1-4 years age group. However, the combined age groups of 5 to 9 years and 10 to 14 years would result in 72.8 % of the cases seen. In the

study by Lopez et. Al, the majority of the patients during the surveillance period from 2011 to 2014 were children aged 15 or under at 68%.⁶ This is probably that children are more exposed to the environment wherein the mosquitoes serve as vectors for the disease.

The most common presenting symptom at the time of diagnosis was a seizure, described as generalized tonic-clonic or partial, followed by abnormal behavior and altered sensorium. This is similar to the study done by Chen. Et. Al in Taiwan which showed that fever and altered sensorium were the most common presenting symptoms.⁸ In our setting, seizures were considered a medical emergency that warrants prompt medical intervention.

The most common pathogen that was isolated in this study was Japanese encephalitis virus followed by dengue and herpes simplex. This may be due to favorable epidemiological factors like a tropical climate with the year-long rainy season, the presence of waterlogged paddy field supporting the profuse breeding of vector mosquitoes, piggeries in close proximity to the residence, non-use of bed nets and outdoor activities of children similar to other Asian countries.^{8,9} The study of Kakoti et. al showed that 233 patients who were admitted from March to December 2012 in the Assam Medical College Hospital in India were due to AES caused by JEV¹. India and Philippines had some similarities in terms of environment and socio-economic status hence rendering their population susceptible to the disease.

This study used the modified Rankin scale as a standardized tool to measure the neurologic outcome of patients prior to discharge. It has been used in several studies in children such as the study of Bigi et. al in India wherein the outcome of acute ischemic stroke in 128 children and 199 adults were compared.¹¹ The modified Rankin scale was used by

Misra et al to determine neurological outcomes of pediatric patients with central nervous system infection in a neurological critical care unit in India.¹² There were several etiologies of the central nervous infection seen in the study such as tuberculous meningitis (47%), viral meningitis (37%), pyogenic meningitis (11%) and fungal meningitis (5%). After a 3-month follow-up period, there were 62% who were fully recovered, 27% who were severely disabled, and 11% who died.¹⁴ The use of a standardized tool for assessing clinical outcome prior to discharge, such as the Modified Rankin scale may be useful in comparing outcomes across different populations presenting with acute viral encephalitis.

The outcome seen in the study showed that there were no deaths in the Japanese encephalitis group was probably because of prompt medical attention is given to most patients who were brought in the hospital within 1 week when the symptoms appeared. However, it was not known whether patients with severe diseases experienced rapid disease progression and died at home before they could be brought to the hospital. In the study of Kakoti et. al, there were 9 deaths and a high case fatality rate (14.47%) attributed to late medical intervention because most cases sought medical attention more than 7 days from the onset of symptoms¹. There was an over-all 6%-7% mortality seen in JEV cases in the systematic review by Lopez. et al. This rate, however, was still considered underreported since some patients who came in where severely-ill that obtaining a viral study was deemed impossible. Some patients were also taken home by their relatives prior to their demise hence the underestimation of the true case fatality rate⁶. In this study, all of the deaths occurred in patients with dengue probably because they already in severe shock when they were brought to the hospital.

The data provided by this study can be used to prevent further transmission of acute encephalitis syndrome effectively through vaccination. The inclusion of the Japanese encephalitis vaccine in the national immunization program is highly considered¹². The government should provide vaccines especially in rural areas wherein children at a greater risk acquiring the infection. However, it is important to note that Dengue encephalitis is also a significant cause of morbidity and mortality hence continued surveillance in Dengue-prone areas should be done and clean up drive should be intensified. As noted in the study of Lopez et. al. stated that the WHO recommends that there is a one-time campaign in a locally-targeted population followed by the JE vaccine in a routine vaccination program especially those under 15 years old and areas of a high proportion of cases seen is considered most effective. There is a need for continued surveillance over time so that the disease quantity can be correctly monitored⁶. All travelers going to endemic areas should protect themselves from mosquito bites by limiting outdoor activities from dusk to dawn wherein they are deemed to be active because of the cooler temperature and wearing appropriate clothes to cover their body. The use of insect repellants containing DEET, IR3535, picaridin or oil of lemon eucalyptus provides adequate protection.¹⁰

LIMITATIONS OF THE STUDY

One limitation of this study was the failure to obtain data for all of the patients identified with acute viral encephalitis due to missing medical records. Only 64 out of the 75 eligible patients' charts were reviewed. Second, there were several patients who did not have viral studies done because of insufficient funds. During 2011-2012, there was an ongoing study done in RITM using the

Panbio test kit comprising of Japanese B and Dengue titers hence it was widely used during that time. The succeeding years showed a decline in the number of specimens sent for viral studies in RITM. As of the present time, our hospital laboratory can only perform limited serologic testing for selected viral pathogens. We have no facilities to perform viral cultures on CSF or other specimens that could be very useful in determining the etiology. Another limitation was the inconsistent reporting of the physical and neurological findings in the patients' medical records prior to their. The incomplete reporting may have affected the assessment of the final outcome of the patients at the time of discharge.

CONCLUSION

Acute encephalitis syndrome has a widespread distribution in our country, with the highest number of cases coming from Region IV. The majority of cases were noted in the 1-4 year age group and commonly in males. Seizure, abnormal behavior, and altered sensorium were the most common presenting symptoms at the time of diagnosis. The most common viral pathogen was Japanese encephalitis virus, followed by dengue and herpes simplex virus. There were 3 deaths, giving a case fatality rate of 4.69%. Majority of patients had a good clinical outcome and there was no significant difference in the outcomes of patients with Japanese encephalitis compared to those with other viral etiologies.

RECOMMENDATIONS

It is crucial that for all cases of suspected acute viral encephalitis or acute encephalitis syndrome, CSF specimens should be submitted to the national reference laboratory located in the Research Institute for Tropical Medicine for viral

studies. This will give a more accurate picture of acute viral encephalitis in the country.

There should be a multicenter review involving more hospitals so that a greater number of patients can be included. A standardized data collection should be emphasized especially prior to discharge hence the use of modified Rankin scale is advised. There should also be a prospective study involving longer follow-up of patients with acute viral encephalitis to validate the use of the modified Rankin scale.

REFERENCES

1. Kakoti G, Dutta P, Das BR, Borah J, Mahanta. Clinical profile and outcome of Japanese encephalitis in children admitted with acute encephalitis syndrome. Biomed Research International; Volume 2013; Article ID 152656, 5 pages. <http://dx.doi.org/10.1155/2013/152656>
2. Kumar R, Tripathi R, Singh R, Bannerji G. Clinical features in children hospitalized during the 2005 epidemic of Japanese encephalitis in Uttar Pradesh, India. Clinical Infectious Diseases 2006; 43 (2): 123-131.
3. Suryawanshi SD, Dube AH, Khadse RK, Jalgaonkar SV, Sathe PS, Zawar SD, Holay MP. Clinical profile of chikungunya fever in patients in a tertiary care centre in Maharashtra, India, PLOS One, January 2014: pp. 438-431
4. Lim J, Gatchalian S, Capeding R, Profile of Pediatric patients with Dengue Fever/ Dengue Hemorrhagic fever over a five year period (2000-2004). Pediatric Infectious Disease Society of the Philippines Journal 2010; 11: 26-35
5. Department of Health, National Epidemiological Center, Philippine Integrated Disease Surveillance, and Response, "Annual Report 2014"
6. Lopez AL, Aldaba JG, Roque VG, Tandoc, AO , Sy AK, Espino FE, DeQuiroz-Castro M, Jee Y, Ducusin MJ, Fox KK. Epidemiology of Japanese Encephalitis in the Philippines: A Systematic Review. PLOS Neglected Diseases 2015: 1935-2735
7. Potula R., Badrinath S., and Srinivasan S., Japanese encephalitis in and around Pondicherry, south India: a clinical appraisal and prognostic indicators for the outcome. Journal of Tropical Pediatrics 2000; 49 (1): 48-53.
8. Chen K-M., Tsai H-C., Sy C-L. et al., "Clinical manifestations of Japanese encephalitis in southern Taiwan," Journal of

- Microbiology, Immunology and Infection 2009; 42 (4): 23-29.
- 9. Center for Disease Control and Prevention (CDC), "Question and answer about Japanese Encephalitis," cited March 2013, Available from <http://www.cdc.gov/japanesencephalitis/qa/index.html>
 - 10. World Health Organization (WHO), "Immunization, vaccines and biological," cited March 2013, Available from http://www.who.int/immunization/topics/japanese_encephalitis/en/index.html.
 - 11. Bigi S, Fischer U et al. "Acute ischaemic stroke in children and young adults: Differences in clinical presentation, aetiology, and outcome" American Neurological Association Journal 2011; 70: pp 245-254
 - 12. Philippine Pediatric Society, Pediatric Infectious Disease Society of the Philippines, Philippine Foundation for Vaccination "Childhood Immunization Schedule 2015"
 - 13. Misra U, Kalita J. Spectrum, and outcome predictors of central nervous system infection in a neurological critical care unit in India: A retrospective review" Transactions of the Royal Society of Tropical Medicine and Hygiene 2014; 108 (3): 141-146.