Predictors of Death and Prolonged Hospital Length of Stay in Dengue Fever Patients Admitted to a Tertiary Hospital in Makkah.

Wael Shahin[1], Mohamed Aly[2]

[1] *Gastroenterology, Hepatology and Infectious Diseases Department, Faculty of Medicine, Benha University, Benha, Egypt.*

[2] *Internal Medicine Department, Faculty of Medicine, South Valley University, Qena, Egypt.*

Corresponding Author
Wael A. Shahin, M.D.

Mobile:
00966507971162

E mail:
waelzaki1@hotmail.com

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Background and study aim: Dengue fever is one of the commonest viral infections in tropical and subtropical areas and its main burden is related to patient's mortality and cost of hospital admission. Our aim was to study dengue fever patients admitted to a tertiary hospital as regards the predictors of patient's death and prolonged hospital length of stay (HLOS).

Patients and methods:This study included 123 patients. They were investigated for demographic, clinical and laboratory data that could predict the mortality and prolonged HLOS cases.

Results: Ninety one patients were males (74%) and average age was 30.6 ± 13.8 years. 119 patients (96.7%) improved and 4 patients (3.3%) died in the hospital. Out of the 119 patients, 38 patients (30.9%) were discharged after 5 days. Statistically significant predictors of prolonged HLOS (> 5 days) were leucopenia, INR > 1.25 and Creatine Kinase (CK) serum level > 488 IU/dl. Predictors of patient's death were male, non Saudi patients, age > 41.5 years, and complicated case (ICU admission , CNS hemorrhage and renal and/or liver failure). On multivariate logistic regression analysis; the laboratory independent predictors of death were AST > 610 IU/dl, ALT > 150 IU/dl, PT > 16.65 sec and INR > 1.4.

Conclusion: In a tertiary hospital in Makkah, the mortality rate of dengue fever patients was 3.3%.Predictors of patient's death were old age, male, non-Saudi patients, ICU admission, CNS hemorrhage, renal and liver failure and on multivariate logistic regression analysis, laboratory predictors were high serum levels of AST, ALT, PT and INR. About 31% of dengue fever patients needed hospital admission for >5 days and the statistically significant predictors were leucopenia, high INR and high CK serum levels.

INTRODUCTION

A dengue epidemic is one of the most important public health problems in the tropical and subtropical areas[1]. The geographical spread and severity are increasing dramatically, about 2.5 to 3 billion people are living in over 100 countries where dengue viruses can be transmitted. It is estimated that, there is 50 million new dengue infections happened every year, with 500,000 cases of DHF and at least 12,000 deaths. Epidemics of dengue like disease were reported in the Arabian Peninsula in the late 19th century (1870–1873), the disease appeared in Mecca, Madina, and Jeddah[2,3] . Results of a Saudi Arabian Ministry of Health (MOH) study showed that during the period 2006—2007, 1551 notified cases with an overall case-fatality rate of 0.52% [4]. Serious complications were uncommon, development of dengue hemorrhagic fever and dengue shock syndrome were rare but had a fatality rate of 2% to 5% [5]. Apart from fatality, the main burden is related to the cost of hospital admission.

This study was done on dengue fever patients admitted to Al Noor Hospital, Makkah during the year 2009; the aim of the study was to investigate the predictors that can help in the recognition of fatality cases and prolonged hospital length of stay cases, so the health care providers can early recognize the serious cases that need special care and can recognize the cases that can be safely discharged early.

PATIENTS AND METHODS

Study site and population:

This was a cross sectional, single center retrospective observational study done on dengue fever patients admitted to Al Noor specialist Hospital, Makkah, during the year 2009. Al Noor Specialist Hospital is a 600-bed, well-equipped hospital, it is the main hospital in Makkah.

Study design

All patients were diagnosed as a case of dengue fever and implemented on the Hospital Information System (HIS) according to the disease coding system ICD-10 AM (International Classification of Disease-10, Australian Modification), version 2006. Diagnosis depends on clinical presentation, serology and PCR study. The data studied included the demographic features (age, sex and nationality), Laboratory investigations (complete blood count, liver function tests, coagulation profile and serum Creatine Kinase (which is usually related to muscle injury). The hospital length of stay (HLOS) was the number of admission days including the admission and the discharge days. At Al Noor specialist hospital, dengue fever patients admitted for more than 5 days were considered to have "prolonged HLOS".

Course of the illness

Patients were discharged from hospital according to WHO criteria which include: absence of fever for at least 24 hours without the use of antipyretics, return of appetite, visible clinical improvement, good urine output, minimum of three days after recovery from shock, no respiratory distress, no ascites and platelet count of more than 50 thousands/cmm [6].

Statistical analyses:

The analysis was performed in SPSS version 17 (SPSS Inc., Chicago, IL, USA). Mean and standard deviation were calculated for quantitative variables and frequencies and percentages for qualitative variables. The Chi-square test was used to see the association among qualitative variables and student's *t*- test was used to see the differences in quantitative variable. Multiple logistic regression was used to predict a model of factors associated with mortality in patients with dengue fever. *P* value < 0.05 was considered statistically significant.

RESULTS

A total of 123 dengue fever patients were admitted to Al Noor Specialist Hospital, the males were 91 patients (74%), mean age of patients was 30.6 ± 13.8 years and 100 patients were Saudi (81%). Hospital Length of stay (HLOS) ranged from 2 to 14 days (mean ± SD 4.76 ± 2.25 days). Eighty one patients (65.8%) were discharged within 5 days, 38 patients were discharged after 5 days (30.9%) and 4 patients died during admission (3.3%) Figure (1).

When comparing the patients with regular (up to 5 days) and prolonged HLOS (more than 5 days), it is found that no significant difference between the two groups except low WBCs (p 0.00), high INR (p 0.03) and high CK serum level (p 0.03), (table 1), the cut off value for CK level was 488 IU/dl (sensitivity 100%, specificity 63.4%) and for INR the cut off value was 1.25 (sensitivity 100%, specificity 98.6%). Table (2)

Four patients died during admission, All patients were males (100%), only one was Saudi (25% vs. 83% p 0.003), and they were significantly older in age (p value 0.04), the number of admission days was (1, 2, 2 and 5 days, median 2 days and mean 3.3 days). Clinically; all mortality cases were admitted at the intensive care unit (ICU): two patients developed acute renal failure, one patient developed acute liver failure and one had septic shock. Three patients (75%) developed significant haemorrhage; (one had massive GI haemorrhage, one had subarachnoid haemorrhage and one had encephalitis with multiple small cerebral haemorrhagic spots). The laboratory results showed that: Hb was significantly lower (p value 0.029); WBCs were significantly higher (p value 0.000), marked reduction in platelet count (p 0.013), AST, ALT, PTT, PT and INR were significantly higher in mortality cases (p value 0.000), table (3). Independent predictors of patient death using logistic regression analysis were high AST and ALT serum levels and prolonged PT , table (4). Table (5) showed the cut off value for predictors of patient's death; they were the age (41.5 years), AST (610.5 IU/dl), ALT (150.5 IU/dl), PT (16.65 sec) and INR (1.4); sensitivity and specificity were demonstrated.

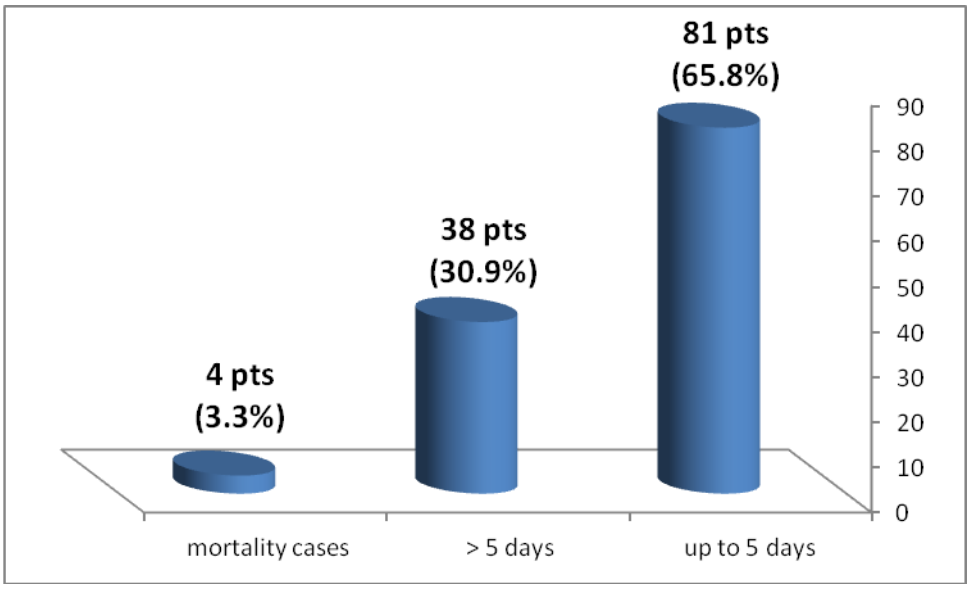

Figure (1): Number of dengue fever patients as regards early and late discharge and fatality cases.

Table (1): comparison between early and late discharge dengue fever patients.

Parameter (no, %), (m ± SD)	LOS up to 5 d 81pt (65.8%)	LOS > 5 days 38 pt (30.9%)	P value
Age (yr)	31.1 ± 14.1	33.5 ± 16.1	>0.05
Male (no, %)	59 (72.8%)	28 (73.7%)	>0.05
Saudi (no, %)	67 (82.7%)	32 (84.2%)	>0.05
Hb (gm %)	13.96 ± 1.7	13.6 ± 1.8	>0.05
WBCs (10^3/cmm)	3.3 ± 1.4	2.9 ± 1.2	0.000*
Plat (10^3/cmm)	96.6 ± 43	100.2 ± 62.3	>0.05
AST (IU/ml)	117 ± 112	151 ± 145	>0.05
ALT (IU/ml)	98 ± 105	101 ± 88	>0.05
PTT (sec)	37.1 ± 5.6	37.4 ± 6.3	>0.05
PT (sec)	11.7 ± 1	12.3 ± 1.2	>0.05
INR	0.96 ± 0.1	1 ± 0.1	0.03*
CK	506 ± 519	1162 ± 1672	0.03*

M mean, SD=standard deviation

ALT=alanine aminotransferase *(normal value < 40 U/L*)

AST=aspartate aminotransferase *(normal value < 40 U/L)*

PTT=partial thromboplastin time

WBCs=white blood cells

Table (2): cut off values for predictors of patient's prolonged HLOS.

parameter	value	sensitivity	specificity
CK (TOTAL)	488 IU/dl	100%	63.4%
INR	1.25	100%	98.6%

Table (3): Comparison between dengue fever discharged patients and mortality cases.

Parameter/ No (%)	Discharged patients 119 (96.7%)	Mortality cases (4 pt) (3.3%)	P value
Age yr (m ± SD)	30.14 ± 13.4	44.3 ± 20.1	0.04*
Male (no, %)	87 (73%)	4 (100%)	>0.05
Saudi (no, %)	99 (83%)	1 /4 (25%)	0.003*
Hb (gm %)	13.4 ± 1.9	11.1 ± 4.8	0.029*
WBCs (10^3/cmm)	3.04 ± 1.4	8 ± 4.1	0.000*
Plat (10^3/cmm)	106.2 ± 66	22.5 ± 14.9	0.013*
AST (IU/ml)	129.2 ± 128	5311 ± 4735	0.000*
ALT(IU/ml)	97.3 ± 92.9	2024 ± 1907	0.000*
PTT(sec)	37.4 ± 5.6	78.5 ± 30.2	0.000*
PT(sec)	11.9 ± 0.9	28.9 ± 10.9	0.000*
INR	0.98 ± 0.1	2.5 ± 0.9	0.000*
CK(IU/ml)	655.3 ± 963	1573 ± 904	>0.05

Table (4): Independent predictors for patient death using logistic regression analysis.

parameter		95% C.I.for EXP(B)		Sig
	Exp(B)	Lower	Upper	P value
AST	1.029	1.001	1.058	0.044*
ALT	0.965	0.934	0.997	0.032 *
PT	0.017	0.001	0.549	0.022*

Table (5): cut off values for predictors of patient's death

parameter	value	sensitivity	specificity
Age	41.5 yrs	75%	81.5%
AST	610.5 IU/dl	100%	98%
ALT	150.5 IU/dl	100%	86%
PT	16.65 second	100%	100%
INR	1.4	100%	100%

DISCUSSION

Dengue fever is typically a self-limiting disease, dengue fever patients usually have a very low mortality rate (less than 1%) and survivors usually recover without sequelae and develop immunity to the infecting serotype. In dengue hemorrhagic fever (DHF), the mortality rate varies from 2 - 5% in treated cases and up to 50% in untreated cases[7].

In a study on 1695 dengue fever patients from 8 American and Asian countries, the average illness lasted 11 days for hospitalized patients. Overall mean costs were more than double for hospitalized cases[8].

In this study, male patients were more infected (74%); this is also noticed in other studies from Makkah and Jeddah (males were 51%- 67%) [9,10,11,12]. Contrary to that, females

were more often infected than males in a study from Brazil (females 59.3%)[13]. Male preponderance may be related to changes in immune system related to gender[14]. Also, females were less exposed to mosquitoes[15] .

In this study, the mean age of patients was 30.6 ± 13.8 years, this is close to other studies from Makkah and Jeddah (23 ± 9 years [11] , 25.6±16.1 years[10] and 27.6 ±11.2 years[12]. In South and South East Asia, dengue fever is an infectious disease of children and the peak age ranged from 5 to 10 years[16]. In Latin America, dengue fever is a disease of adults[17], Saudi Arabia is a part of Asia but the age pattern of infection is related to Latin American pattern, and this may be due to the dengue genotype prevalent[10].

Fatality rate in this study was 3.3%, in two studies from Saudi Arabia; the fatality rate was 0.5 and 0.6%[18,10]. Internationally, the mortality rates were 1.3% in Indonesian study[19], 6% in Cuban epidemic[7] and 0.06% and 1.7% in two studies from Singapore[20,21]. The variation in the case fatality rate depends on the percentage of severe cases included in the study.

In this study, all patients died were males (100%) and median age of 46.5 years (m ± SD: 44.3 ± 20.1), all were admitted to ICU and death occurred at a median of 2 days after admission to ICU (range 1 – 5 days). In a study from Singapore, the median age of patients who died was 59 years and 67.9% of patients were males, also, 70% of them were admitted to ICU and the median duration of ICU stay was 3 days (range, 1-32 days)[22].

In this study, mortality cases had significantly low HB and platelets and high WBCs, AST, ALT, PTT, PT and INR (table 3). On using logistic regression analysis, the independent predictors of patient death were AST, ALT and PT levels (p=0.04, p=0.3 and p=0.02 respectively) (table 4) and table (5), showed the cut off values of age (41.5 yrs), AST (610.5 IU/dl), ALT (150.5 IU/dl), PT (16.65 sec) and INR (1.4). Similar results were observed in a study from Pakistan where the mortality predictors were; high WBCs count (p=0.02), PTT (56.8 versus 36.8, p=0.01) and ALT (802 versus 176, p=0.01) and on multivariate logistic regression analysis, ALT > 300 *IU/*dl, bleeding, an altered mental status and shock at presentation were all significantly associated with mortality (p=0.008, p<0.001, p<0.001, p<0.001, respectively)[23] . The impaired level of consciousness in dengue patients is usually related to dengue encephalopathy[24,25]., which may be due to direct dengue encephalitis or associated liver failure[24].

In this study, clinical predictors of death during admission were old age, male, non Saudi patients, admission to ICU, developing haemorrhage especially CNS haemorrhage and acute renal and/or liver failure. These results are supported by reports other parts of the world where the following mortality predictors were listed: old age (Taiwan[26], Singapore[21] and Puerto Rico[27], spontaneous bleeding[28], the presence of chronic diseases[21], renal disease [29] and ethnicity[21]. In a study from Singapore[22], clinical predictors of death were platelet count <20 × 10^9/L, acute renal impairment, impaired consciousness and severe hepatitis, while in a study from Pakistan, high white cell count, uremia, acidosis and deranged liver function were the laboratory predictors of death[30].

One of the important laboratory predictors of patient's death is liver damage which manifests as increase in AST and ALT serum levels and deranged coagulation parameters. In persons with fatal dengue hepatitis, direct virus infection was demonstrated in more than 90% of hepatocytes and Kupffer cells[31,32]. There was a correlation between liver enzymes and the severity of dengue infection and in patients who presented with encephalopathy, AST and ALT values usually exceeded 200 IU/dl[33,34]. In rare cases, dengue fever may present as an acute liver failure[35]. In contrast to other viral infections which involve the liver, dengue hepatitis is associated with AST higher than ALT levels[33,29,10], this difference could be due to the release of AST from skeletal muscle as muscle damage in dengue infections has been reported, this muscle damage may also explain the increased CK serum levels[36].

In this study three out of four mortality cases were non Saudi, the foreigners are more prone to poorer prognosis[10,11] , this may be related to the lower socioeconomic status and often living in poorer areas with inadequately developed infrastructures[11] which increases the incidence and prevalence of dengue and dengue haemorrhagic fever[37,38] .

The strength of this study is that, to our knowledge, it is the first study from Saudi Arabia which identified the factors associated with mortality in a multivariate analysis. There were some limitations; it is a single center study, it is of retrospective type and the small number of mortality cases.

CONCLUSION

Identification of prolonged HLOS predictors may help the health care providers to safely discharge patients early and to decrease the final cost of care of dengue fever patients, these predictors were leucopenia, INR < 1.25 and CK serum level < 488 IU/dl. Clinical predictors of death were non Saudi male patients, aged above 41.5yrs, ICU admission, CNS hemorrhage and acute renal or liver failure. Mortality laboratory predictors were high WBCs, AST > 610 IU/dl, ALT >150 IU/dl, INR >1.4 and PT> 16.65; patients presented with these symptoms should be admitted in high dependency units.

Abbreviations:

HLOS: hospital length of stay.

AST: Aspartate Transaminase.

ALT: Alanine Transaminase.

CK: Creatine Kinase.

PT: prothrombin Time.

INR: International Ratio.

IU: International Unit.

Dl: Deciliter.

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REFERENCES

1. Gibbons RV, Vaughn DW. Dengue: an escalating problem. *BMJ* 2002; 324: 1563–1566.
2. World Health Organization. Report on dengue prevention and control. WHO, 55th World Health Assembly, 4 March 2002, document A55/19.
3. World Health Organization (WHO) and the Special Programme for Research and Training in Tropical Diseases (TDR) . Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: WHO; 2009
4. El Musharaf N, Akbar N. Dengue and dengue hemorrhagic fever epidemic in Jeddah 2006—2007. In: The Second International Conference on Dengue and Dengue Haemorrhagic Fever; 2008.
5. Shepherd MS, Patrick BH, William HS. "Dengue Fever." eMedicine. Eds. Martin J. Wood, et al. 4 Apr. 2002. Medscape. 10 Sep. 2004 <http://emedicine.com/med/topic528.htm>.
6. World Health Organization. Guidelines for treatment of dengue fever/dengue haemorrhagic fever in small hospitals. New Delhi: World Health Organization, Regional Office for South-East Asia 1999; p. 2-3.
7. Anderson KB, Chunsuttiwat S, Nisalak A, Mammen MP, Libraty DH, Rothman AL. Burden of symptomatic dengue infection in children at primary school in Thailand: a prospective study. *Lancet* 2007; 28, 369 (9571): 1452-9.
8. Suaya JA, Shepard DS, Siqueira JB ,Martelli CT, Lum LC, Tan LH, et al. Cost of dengue cases in eight countries in the Americas and Asia: a prospective study. *Am J Trop Med Hyg.*2009; 80(5): 846-55.
9. Kholedi A.A.N., Balubaid O, Milaat W, Kabbash I.A., Ibrahim A. Factors associated with the spread of dengue fever in Jeddah Governorate, Saudi Arabia. *EMHJ* (Eastern Mediterranean Health Journal) 2012; 18 (1): 15 – 23.
10. Shahin WA, Nassar AH, Kalkattawi M, Bokhari HA. Dengue fever in a tertiary hospital in Makkah, Saudi Arabia. *Dengue Bulletin* 2009; 33: 34 – 44.
11. Said SM, Elsaeed KM, Alyan Z. Benign Acute Myositis in Association with Acute Dengue Viruses' Infections. *Egypt J. Neurol. Psychiat. Neurosurg* 2008 45(1): 193-200.
12. Ayyub M, Khazindar AM, Lubbad EH, Barlas S, Alfi AY, Al- Ukayli A. Characteristics of dengue fever in a large public hospital, Jeddah, Saudi Arabia. *Journal of Ayub Medical College, Abbottabad* 2006;18(2):9—13.
13. Cordeiro MT, Schatzmayr HG, Nogueira RM, Oliveira VF, Melo WT, Carvalho EF. Dengue and dengue hemorrhagic fever in the State of Pernambuco, 1995–2006. *Revista da Sociedade Brasileira de Medicina Tropical* 2007; 40:605–611.

14. Halstead S. Observations related to pathogenesis of dengue hemorrhagic fever. IV. Relation of disease severity to antibody response and virus recovered. *Yale Journal of Biology and Medicine* 1970; 42:311–328.
15. Goh K.T. Changing epidemiology of dengue in Singapore. Lancet 1995; 346:1098.
16. Aggarwal A, Chandra J, Aneja S, Patwari AK, Dutta AK. An epidemic of dengue haemorrhagic fever and dengue shock syndrome in children in Delhi. *Indian Pediatr* 1998; 35(8): 727 – 32.
17. Teixeira MG, Costa MC, Barreto ML, Mota E. Dengue and dengue haemorrhagic fever epidemics in Brazil: what research is needed based on trends; surveillance, and control experiences? *Cad Saude Publica* 2005; 21: 1307 – 15.
18. Surveillance report. Jeddah, Saudi Arabia, Ministry of Health, Department of Communicable Diseases 2007.
19. Teixeira MG, Costa MC, Coelho G, Barreto ML. Recent shift in age pattern of dengue haemorrhagic fever, Brazil. *Emerging Infectious Diseases* 2008; 14(10):1663.
20. Ministry of Health Singapore: Communicable Diseases Surveillance in Singapore. Singapore; 2008.
21. Lahiri M, Fisher D, Tambyah PA. Dengue mortality: reassessing the risks in transition countries. *Trans R Soc Trop Med Hyg* 2008; 102(10):1011-1016.
22. Leo YS**,** Thein TL**,** Fisher DA**,** Low JG**,** Oh HM**,** Narayanan RL , et al. Confirmed adult dengue deaths in Singapore 5-year multi-center retrospective study**.** 2011:http://www.biomedcentral.com/bmcinfectdismhtml:filehttp://www.biomedcentral.com/1471-2334/11/123
23. Almas A, Parkash O, Akhter J. clinical factors associated with mortality in dengue infection at a tertiary care center. *Southeast Asian J Trop Med Public Health* 2010; 41 (2): 333-340.
24. Cam BV, Fonsmark L, Hue NB, Phuong NT, Poulsen A, Heegaard ED. Prospective case-control study of encephalopathy in children with dengue hemorrhagic fever. *Am J Trop Med Hyg* 2001; 65(6):848-851.
25. Malavige GN, Ranatunga PK, Jayaratne SD, Wijesiriwardana B, Seneviratne SL, Karunatilaka DH. Dengue viral infections as a cause of encephalopathy. *Indian J Med Microbiol* 2007;25(2):143-145.
26. Lee IK, Liu JW, Yang KD. Clinical characteristics and risk factors for concurrent bacteremia in adults with dengue hemorrhagic fever. *Am J Trop Med Hyg* 2005; 72 (2): 221-226.
27. Garcia-Rivera EJ, Rigau-Perez JG. Dengue severity in the elderly in Puerto Rico. *Pan Am J Public Health* 2003;13: 362–368.
28. Diaz-Quijano FA. Predictors of spontaneous bleeding in dengue patients: a systematic review of the literature. *Investig Clin* 2008; 49: 111-22.
29. Kuo MC, Lu PL, Chang JM, Lin MY, Tsai JJ, Chen YH, Chang K, Chen HC, Hwang SJ. Impact of renal failure on the outcome of dengue viral infection. *Clin J Am Soc Nephrol* 2008; 3(5):1350-1356.
30. Ahmed S, Arif F, Yahya Y, Rehman A, Abbas K, Ashraf S, Akram DS. Dengue fever outbreak in Karachi 2006. A study of profile and outcome of children under 15 years of age. *J. Pakistan Med. Assoc* 2008; 58: 4 – 8.
31. de Macedo FC, Nicol AF, Cooper LD, Yearsley M, Pires AR, Nuovo GJ. Histologic, viral, and molecular correlates of dengue fever infection of the liver using highly sensitive immunohistochemistry. *Diagn Mol Pathol* 2006; 15(4):223-8.
32. Shah I. Dengue and liver disease. *Scand J Infect Dis* 2008; 40(11-12):993-4.
33. Nimmannitya S, Thisyakorn U, Hemsrichart V. Dengue haemorrhagic fever with unusual manifestations. *Southeast Asian J Trop Med Public Health* 1987; 18(3):398-406.
34. Mohan B, Patwari AK, Anand VK. Hepatic dysfunction in childhood dengue infection. *J Trop Pediatr* 2000; 46(1):40-43.
35. Vinodh BN, Bammigatti C, Kumar A, Mittal V. Dengue fever with acute liver failure. *Case reports* 2005; 51(4):322-323.
36. Davis JS, Bourke P. Rhabdomyolysis associated with dengue virus infection. *Clinical infectious disease* 2004; 38, e 109 – e111.
37. Kaplan JE, Eliason DA, Moore M, Sather GE, Schonberger LB, Cabrera-Coello L, et al. Epidemiologic investigations of dengue infection in Mexico. *American Journal of Epidemiology* 1983; 117:335–343.
38. Brunkard JM, Lopez JL, Ramirez J, Cifuentes E, Rothenberg SJ, Hunsperger EA, Moore CG, Brussolo RM, Villarreal NA, Haddad BM. Dengue fever seroprevalence and risk factors, Texas-Mexico border, 2004. *Emerging Infectious Diseases* 2007; 13 (10):1477–1483.

Peer reviewer :Mohamad Emam ; Professor of Tropical Medicine , Faculty of Medicine, Zagazig University, Egypt.**Editor: Tarik Zaher**; Professor of Tropical Medicine , Faculty of Medicine, Zagazig University, Egypt.