Asian Pacific Journal of Tropical Disease

journal homepage: http://www.apjtcm.com

Short communications https://doi.org/10.12980/apjtd.7.2017D7-208

Aggregate organ failure rates among dengue patients in Malaysia: Five years' risk analysis (2010–2015)

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ARTICLE INFO

Article history:
Received 11 Sep 2017
Received in revised form 26 Sep 2017
Accepted 13 Oct 2017
Available online 29 Nov 2017

Keywords:
Dengue haemorrhagic fever
Dengue shock syndrome
Multiple organ damage
Respiratory failure
Cardiovascular failure
Haematological failure

ABSTRACT

Objective: To estimate the incidence of dengue-induced organ failure form 2010–2015 in Malaysia.
Methods: Data were extracted from the Malaysian Registry of Intensive Care published in June 2016. Analysis of proportions was carried out using StatsDirect software. Binary data for the outcomes available from the included studies were analyzed using StatsDirect software, using random effect model.
Results: It is noteworthy that there was a drop in all complications among dengue patients at 2011. Except in year 2011, 52% [0.52 (CI 95% 0.49–0.56)] of the patients with dengue developed hematological failure.
Conclusions: The statistics indicate that dengue has increasingly led to cardiovascular, neurological, renal and hematological failure, as indicated from an increasing trend from year 2011–2015.

1. Introduction

Dengue is one of the world's main public health challenges. There is almost 4 billion people who are at risk of having dengue infestation and its complications[1]. The World Health Organization (WHO) estimates that about 50–100 million cases are reported every year, with an annual death rate of 20 000[2]. The incidence rate of dengue in Malaysia had increased five-fold from 31.6 cases/100 000 in 2000 to 159.7 cases/100 000 in 2010[3]. Between 2013 and 2014 there was a huge increase of 151% in the number of dengue cases in Malaysia (108 698 compared to 43 346) [4]. The number of dengue cases increased further in 2015, namely from 108 698 to 120 836, which is an increase of 11.2%. Since 2001, the fatality rate has been 2 to 3 per 1 000 dengue cases[3]. This massive rise of dengue incidence in Malaysia has further increased the cost and complications associated with dengue infestation, in particular among critically ill patients with multiple organ failures.

Dengue-induced organ failure is a highly neglected intricacy and is accompanied by poor prognosis. To the best of our knowledge, there are no studies evaluating the association of

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Foundation Project: Supported by LESTARI research grant, Ministry of Higher Education and Universiti Teknologi MARA (UiTM), Malaysia (Grant No. 600-IRMI/DANA 5/3/LESTARI [0006/2016]).
The journal implements double-blind peer review practiced by specially invited international editorial board members.

organ failure with dengue infection in Malaysia. Several studies in different regions including tropical and sub-tropical countries demonstrated that organ failure during dengue infection has a considerable burden on patients and healthcare systems in the form of significant morbidity, longer hospital stays and even mortality. Thus, it is imperative to evaluate the relationship or association of organ failure with dengue infection, especially in a country like Malaysia, where dengue infection is a crucial area of interest for health authorities. It is necessary to evaluate the incidence, clinical characteristics and risk factors of organ failure among dengue patients in Malaysia. By doing so, patients with dengue infection can be properly examined for the presence of organ failure and will be treated in a timely manner.

The findings of the current study provide a clinical picture of dengue-induced organ failure in Malaysia, and give a predictive model of dengue-induced organ failure that will increase clinicians' attention for this highly fatal and morbid complication. Moreover, these findings offer direction to health authorities in terms of policy-making to decrease the dengue burden in Malaysia.

2. Methods

Data were extracted from the Malaysian Registry of Intensive Care published in June 2016. Analysis of proportions was carried out using StatsDirect software. Binary data for the outcomes available from the included studies were analysed using StatsDirect software, using random effect model[5].

3. Results and discussion

From 2010 to 2011 (Table 1), the proportion of all types of organ failures among the dengue patients in Malaysia decreased, and then increased from 2012 to 2015 (except a sudden dip in respiratory and hepatic failures in 2015. Overall, the risk of haematological failure remained the highest with a pooled proportion of 0.52 [CI 95% 0.49–0.56] (Figure 1).

Table 1
Organ failure trends among dengue patients from year 2010 till 2015.

Type of organ failure/ Year (N)	With outcome/ organ failure	Total No. of patients with dengue infection	Proportion [CI 95%]
Respiratory failure			
2010	77	1643	0.047 [0.037–0.058]
2011	24	798	0.030 [0.019–0.044]
2012	30	906	0.033 [0.022–0.047]
2013	45	1550	0.029 [0.021–0.039]
2014	192	3261	0.059 [0.051–0.068]
2015	133	3601	0.037 [0.031–0.044]
Cardiovascular failure			
2010	177	1643	0.108 [0.093–0.124]
2011	57	798	0.071 [0.055–0.091]
2012	63	906	0.070 [0.055–0.088]
2013	95	1550	0.061 [0.049–0.074]
2014	196	3261	0.060 [0.052–0.069]
2015	220	3601	0.061 [0.053–0.069]
Neurological failure			
2010	10	1643	0.006 [0.003–0.011]
2011	3	798	0.004 [0.001–0.011]
2012	1	906	0.001 [0.000–0.011]
2013	11	1550	0.007 [0.004–0.011]
2014	13	3261	0.004 [0.002–0.011]
2015	14	3601	0.004 [0.002–0.011]
Renal failure			
2010	15	1643	0.009 [0.005–0.015]
2011	6	798	0.008 [0.003–0.016]
2012	7	906	0.008 [0.003–0.016]
2013	17	1550	0.011 [0.006–0.018]
2014	39	3261	0.012 [0.009–0.016]
2015	65	3601	0.018 [0.014–0.023]
Hepatic failure			
2010	7	1643	0.004 [0.002–0.009]
2011	1	798	0.001 [0.000–0.007]
2012	1	906	0.001 [0.000–0.006]
2013	5	1550	0.003 [0.001–0.008]
2014	13	3261	0.004 [0.002–0.007]
2015	11	3601	0.003 [0.002–0.005]
Haematological failure			
2010	887	1643	0.540 [0.515–0.564]
2011	326	798	0.409 [0.374–0.444]
2012	484	906	0.534 [0.501–0.567]
2013	814	1550	0.525 [0.500–0.550]
2014	1748	3261	0.536 [0.519–0.553]
2015	2056	3601	0.571 [0.555–0.587]

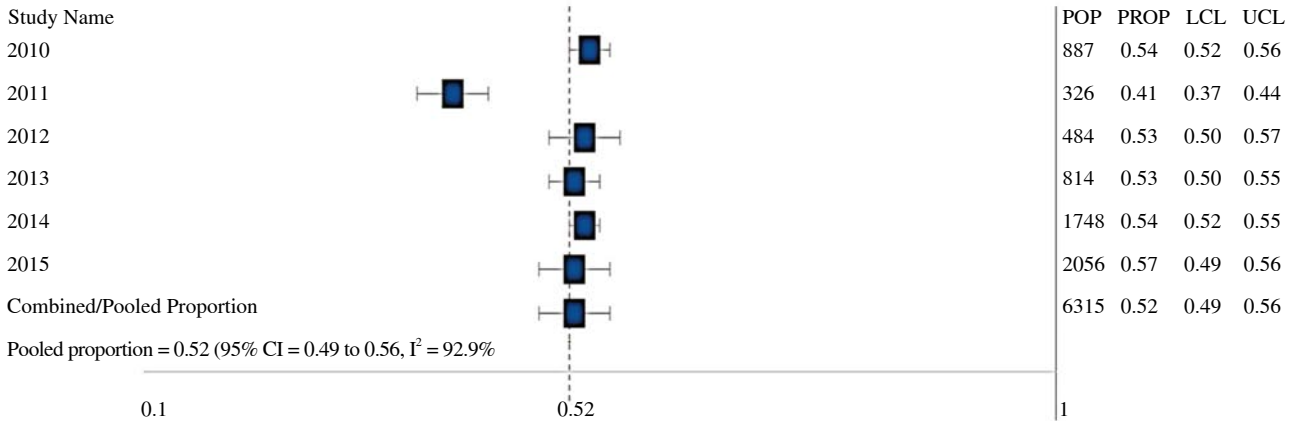

Figure 1. Pooled proportion of hematoligical failure trends among dengue patients from year 2010 till 2015.

The increasing incidence of dengue has substantial impact on global healthcare resources. Dengue-associated complications including multiple involvements of respiratory, renal, hepatic, cardiovascular, coagulation and nervous systems have been documented[6]. Previous studies have demonstrated that dengue patients with multi-organ involvement have more severe manifestations of the illness[7]. Whilst dengue shock syndrome has been identified as a common cause of dengue fatality, severe organ involvement contributed to 69% of dengue deaths in Malaysia[8].

The drastic escalation in the number of dengue cases seen in Malaysia over the last three years may have primarily contributed to the increased trends noted in most dengue-related organ failures, as observed in this study. The significant upward trends in the respiratory, cardiovascular, renal and haematological failures could be due to the fact that the associated organs (lung, heart and kidney) are commonly associated with dengue infection[6]. While the liver is frequently involved in dengue infection, changes in annual hepatic failure rates were not significant in the current study cohort[6]. This may be because dengue-associated liver injury usually appears after one week of infection; thus, liver function tests done at earlier dates might not reflect the extent of liver involvement in acute infection[6].

The latest World Health Organization dengue guidelines included central nervous system involvement in the definition of severe dengue infection[7]. Neurological complications were identified in only 4%–5% of the reported dengue cases: these include dengue encephalopathy (due to the liver failure or metabolic disorders), encephalitis or acute disseminated encephalomyelitis (caused by direct virus invasion), neuromuscular complications (*e.g.* Guillain-Barré syndrome), and neuro-ophthalmic involvement (*e.g.* optic neuritis)[8]. The observations from this study are that the change in trend involving neurological failure among the Malaysian dengue patients is insignificant.

The limitation of the current study is the fact that it was conducted using secondary data, and thus the rates of organ failure could have been underestimated. A prospective cohort study would be a better study design to determine the correlations. The general public should take heed of health advice and seek early hospital treatment for suspected dengue cases. They should refrain from self-medicating using traditional remedies, as a delay in proper diagnosis and treatment could lead to a higher risk of dengue haemorrhagic fever and dengue shock syndrome as well as multiple organ damage.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

This work was supported by LESTARI research grant, Ministry of Higher Education and Universiti Teknologi MARA (UiTM), Malaysia (Grant No. 600-IRMI/DANA 5/3/LESTARI [0006/2016]).

References

[1] Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis* 2012; **6**(8): e1760.

[2] World Health Organization. Dengue and severe dengue. Geneva: World Health Organization; 2016. [Online] Available from: http://www.who.int/mediacentre/factsheets/fs117/en/ [Accessed on December 22nd, 2016]

[3] World Health Organization. Update on the dengue situation in the Western Pacific Region. Geneva: World Health Organization; 2015, p. 1-5. [Online] Available from: http://www.wpro.who.int/emerging_diseases/dengue_biweekly_20150922.pdf?ua=1 [Accessed on December 22nd, 2016]

[4] Tong JMG, Tai LL, Tan CC, Lim CH, Ismail NIB. Malaysian Registry of Intensive Care 2015 report. Putrajaya: Malaysian Registry of Intensive Care, Clinical Research Centre, Ministry of Health Malaysia; 2015.

[5] DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**(3): 177-88.

[6] Fernando S, Wijewickrama A, Gomes L, Punchihewa CT, Madusanka SDP, Dissanayake H, et al. Patterns and causes of liver involvement in acute dengue infection. *BMC Infect Dis* 2016; **16**(1): 319.

[7] World Health Organization, Special Programme for Research and Training in Tropical Diseases. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: World Health Organization; 2009. [Online] Available from: http://www.who.int/tdr/publications/documents/dengue-diagnosis.pdf [Accessed on December 22nd, 2016]

[8] Carod-Artal FJ, Wichmann O, Farrar J, Gascón J. Neurological complications of dengue virus infection. *Lancet Neurol* 2013; **12**(9): 906-19.