

Diabetes, cardiac disorders and asthma as risk factors for severe organ involvement among adult dengue patients: A matched case-control study



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1820221170

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MEI 2020

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DENGUE



INTRODUCTION

- » The most important mosquito-borne viral pathogen affecting humans, and is emerging as a major threat to global health
- » Accounts for nearly 75% of the current global dengue disease burden
- » Present with a wide spectrum of clinical symptoms ranging from mild febrile illness through to severe manifestation

DENGUE ± WARNING SIGNS



SEVERE DENGUE

1. Severe plasma leakage
2. Severe haemorrhage
3. Severe organ impairment

CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue

live in /travel to dengue endemic area.

Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confirmed dengue

[important when no sign of plasma leakage]

Warning signs*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

* [requiring strict observation and medical intervention]

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage

leading to:

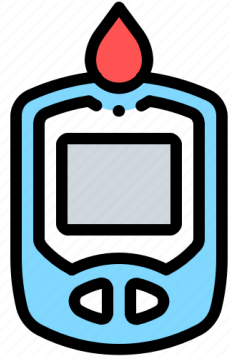
- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding

as evaluated by clinician

Severe organ involvement

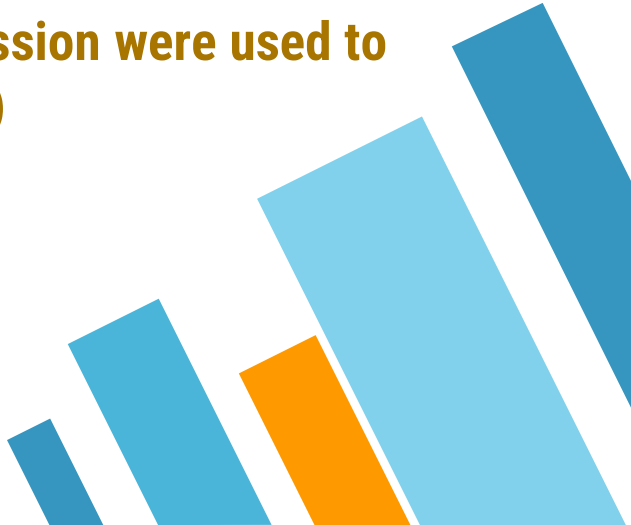
- Liver: AST or ALT \geq 1000
- CNS: Impaired consciousness
- Heart and other organs



To characterize and identify risk factors that are useful to stratify adult dengue patients at a tertiary hospital at risk of progression with severe organ involvement.



METHOD

- » **All adult dengue patients admitted from 1 January 2005 to 31 December 2008 to the Department of Infectious Diseases at Tan Tock Seng Hospital (TTSH)**
 - » **Univariate and multivariate conditional logistic regression were used to calculate crude and adjusted odds ratios (cOR, AcOR)**
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	Controls [^] (N = 865)	%	Cases (N = 174)	%	cOR	p-value	95% CI	95% CI	AcOR	p-value*	95% CI	95% CI
Age (median)	33	(24-42)	37.5	(27-52)	1.03	<0.0001	1.02	1.04	1.01	0.112	0.99	1.03
Age groups												
12-29	342	39.5	51	29.3	1				1			
30-39	241	27.9	45	25.9	1.25	0.318	0.81	1.93	1.25	0.318	0.8	1.95
40-49	167	19.3	30	17.2	1.17	0.531	0.72	1.9	1.07	0.792	0.62	1.72
50-59	77	8.9	18	10.3	1.58	0.128	0.88	2.84	1.11	0.751	0.52	1.99
≥60	38	4.4	30	17.2	5.29	<0.0001	3	9.35	2.75	0.008	1.3	5.8
Gender												
Female	347	40.1	84	48.3	1.41	0.039	1.02	1.96	1.7	0.09	0.95	1.93
Ethnic Groups												
Chinese	593	68.6	114	65.5	1				1			
Malay	84	9.7	20	11.5	1.26	0.403	0.74	2.14	1.09	0.76	0.62	1.93
Indians	86	9.9	17	9.8	1.03	0.915	0.59	1.8	1.15	0.647	0.64	2.07
Others	102	11.8	23	13.2	1.19	0.501	0.72	1.96	1.51	0.129	0.89	2.57
Epidemic Year [^]												
2005	585	67.6	117	67.2								
2006	115	13.3	23	12.2								
2007	75	8.7	16	9.2								
2008	90	10.4	18	10.3								
DPF presentation	5	(4-6)	5	(4-6)	0.89	0.038	0.8	0.99	0.93	0.186	0.83	1.04
IgG positive	241	93.8	70	98.6	1.85	0.579	0.21	16.23	0.88	0.917	0.08	10.2
Detection Assay												
Serology+	582	67.3	114	65.5	1				1			
PCR+	283	32.7	60	34.5	1.10	0.609	0.77	1.55	0.96	0.851	0.66	1.42
Any Pre-existing illness												
Yes	147	17	55	31.6	2.22	<0.0001	1.53	3.22	1.63	0.023	1.07	2.49
Number of Pre-existing illness												
0	718	83.0	117	67.2	1				1			
1	99	11.5	24	13.8	1.42	0.177	0.85	2.36	1.19	0.515	0.70	2.02
≥2	48	5.6	33	19.0	3.92	<0.0001	2.45	6.29	2.90	<0.0001	1.66	5.07
Diabetes	27	3.1	23	12.2	4.75	<0.0001	2.63	8.56	2.21	0.027	1.1	5.02
Hypertension	70	8.1	34	19.5	2.77	<0.0001	1.77	4.33	1.02	0.935	0.54	1.95
Heart Failure	2	0.2	0	0								
Hyperlipidemia	29	3.4	21	12.1	3.65	<0.0001	2.03	6.57	1.46	0.347	0.66	3.22
Cardiac Disorder	9	1	13	7.5	8.59	<0.0001	3.41	21.66	4.30	0.009	1.45	12.78
Lung Disorder	14	1.6	4	2.3	1.43	0.529	0.47	4.34	0.46	0.278	0.12	1.86
Liver Disorder	11	1.3	1	0.6	0.45	0.443	0.06	3.52	0.39	0.383	0.05	3.23
Renal Disorder	3	0.4	1	0.6	1.67	0.658	0.17	16.02	1.25	0.85	0.12	13.2
Asthma	34	3.9	13	7.5	2.05	0.039	1.03	4.04	2.14	0.039	1.04	4.42

	Controls [^] (N = 865)	%	Cases (N = 174)	%	AcOR	p-value	95% CI	95% CI
Classification at Presentation								
DHF/DSS (WHO 1997)	96	11.1	49	28.2	3.11	<0.0001	2	4.85
WS (WHO 2009)	567	65.6	125	71.8	1.38	0.95	0.95	2.02
Classification as final outcome								
DHF/DSS (WHO 1997)	167	19.3	81	46.6	3.95	<0.0001	2.68	5.82
WS (WHO 2009)	656	75.8	152	87.4	1.93	0.008	1.19	3.14
Severe dengue (WHO 2009)	104	12	174	100	62.81	<0.0001	31.37	125.76
Liver involvement	0	0	106	61				
Renal involvement	0	0	60	34.5				
CNS involvement	0	0	23	13.2				
Renal & liver involvement	0	0	15	8.6				
Median LOS (IQR)	4	(3–5)	5	(4–7)	1.4	<0.0001	1.27	1.54
ICU admission	0	0	12	6.9				
IV Fluid	748	86.5	167	96	3.46	0.003	1.53	7.80
Blood transfusion	4	0.5	10	5.8	11.92	<0.0001	3.55	40.6
Platelets transfusion	80	9.3	58	33.3	5.12	<0.0001	3.21	8.16

	Controls^ (N=865)	%	Cases (N=174)	%	cOR	p-value	95% CI	95% CI	AcOR	p-value*	95% CI	95% CI
Diabetes, Cardiac disorder												
No DM, no CD	831	96.07	144	82.76	1				1			
DM, no CD	25	2.89	17	9.77	3.99	<0.0001	2.09	7.61	2.36	0.028	1.10	5.08
CD, no DM	7	0.81	7	4.02	6.73	0.001	2.18	20.83	4.85	0.011	1.43	16.41
DM and CD	2	0.23	6	3.45	18.93	<0.0001	3.74	95.74	8.02	0.019	1.40	45.92
Diabetes, Hypertension												
No DM, no HT	783	90.52	133	76.44	1				1			
DM, no HT	12	1.39	7	4.02	3.66	0.012	1.34	10.04	2.37	0.131	0.77	7.26
HT, no DM	55	6.36	18	10.34	1.96	0.024	1.09	3.51	1.21	0.572	0.62	2.37
DM and HT	15	1.73	16	9.20	5.95	<0.0001	2.85	12.43	2.68	0.035	1.07	6.68
Diabetes, Hyperlipidemia												
No DM, no HL	779	90.06	136	78.16	1				1			
DM, no HL	10	1.16	3	1.72	1.86	0.362	0.49	7.08	1.50	0.562	0.38	5.94
HL, no DM	68	7.86	20	11.49	7.08	0.098	0.92	2.75	5.94	0.436	0.27	1.77
DM and HL	8	0.92	15	8.62	10.89	<0.0001	4.41	26.85	4.25	0.014	1.34	13.52
Cardiac disorder, Hypertension												
No CD, no HT	793	91.68	133	76.44	1				1			
CD, no HT	2	0.23	7	4.02	21.83	<0.0001	4.44	107.30	15.79	0.002	2.87	86.76
HT, no CD	63	7.28	28	16.09	2.62	<0.0001	1.60	4.29	1.41	0.275	0.76	2.61
CD and HT	7	0.81	6	3.45	5.42	0.003	1.75	16.84	2.64	0.141	0.73	9.57
Cardiac disorder, Hyperlipidemia												
No CD, no HL	829	95.84	146	83.91		1				1		
CD, no HL	7	0.81	7	4.02	6.21	0.001	2.03	19.03	4.52	0.016	1.32	15.52
HL, no CD	27	3.12	15	8.62	2.80	0.002	1.44	5.44	1.46	0.357	0.66	3.23
CD and HL	2	0.23	6	3.45	17.28	0.001	3.44	86.91	5.79	0.046	1.03	32.64

Table 2. The risk effect of severe organ involvement with two pre-existing comorbidities.



DIABETES

**CARDIAC
DISORDER**

ASTHMA


AGE

Immunosenescence
Impaired functional

Immune and Endothelial
dysfunction

Severe organ involvement



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- » **Severe organ involvement results in severe dengue disease**
 - » **Age group of 60 years or older, diabetes, cardiac disorders, asthma, and two or more pre-existing comorbidities were independent risk factors of severe organ involvement**
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