# 2015 年台南登革熱大流行: 成醫臨床經驗


成大醫院
National Cheng Kung University Hospital
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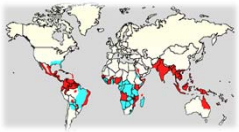
感染病科 柯文謙

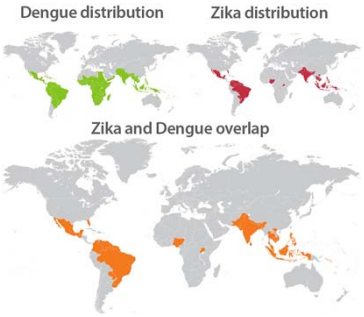
## Global Estimates of Dengue



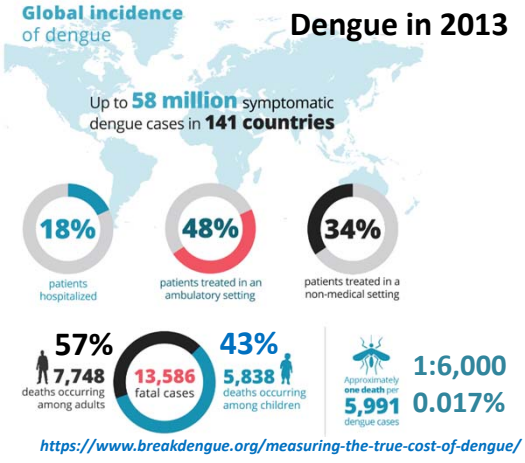
- At risk of dengue: 3.9 billion people in 128 countries
  - esp. Americas, South-East Asia, and Western Pacific
- Underreported and misdiagnosed
- Global estimates: annual 390 million DF cases, symptomatic 96 million (24.6%) cases
  - 566,000 dengue-attributable disability
  - 500,000 require hospitalization
  - 20,000 deaths
  - -> 114 million disability-adjusted life-years (DALYs)

*Dengue vaccine: WHO position paper – September 2018*

## Global Dengue Data

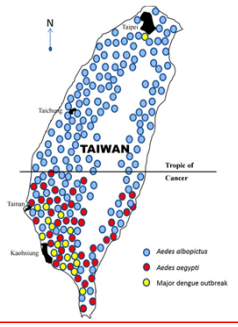


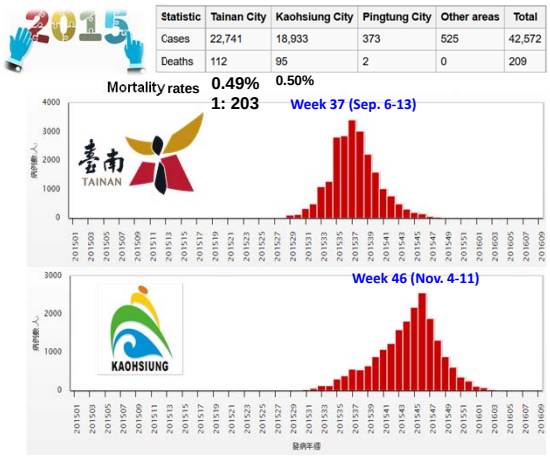

## Dengue in 2013



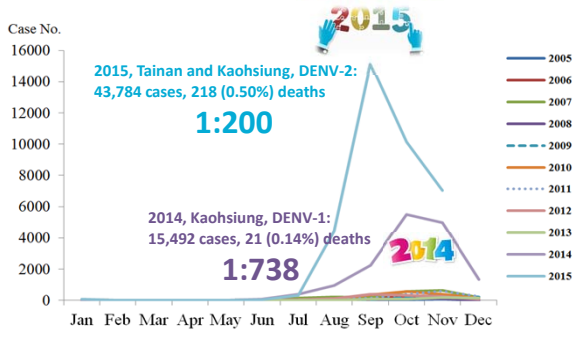

*https://www.breakdengue.org/measuring-the-true-cost-of-dengue/*

# Taiwan Dengue Data

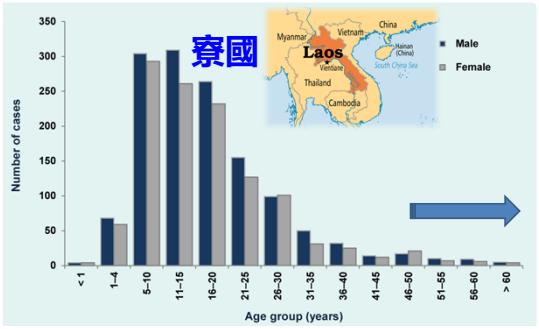



## Confirmed monthly case numbers of dengue fever in Taiwan, from 2005 to 2015




Number of reported dengue cases by sex and age group, Savannakhet Province, the Lao People's Democratic Republic, 2010 ($n$ = 2523)



## 2014 廣東登革熱大流行: 45,171例

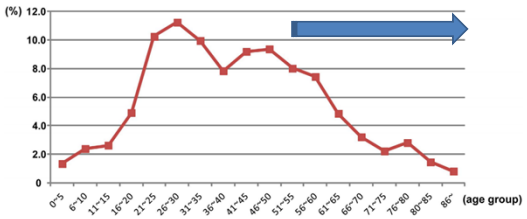


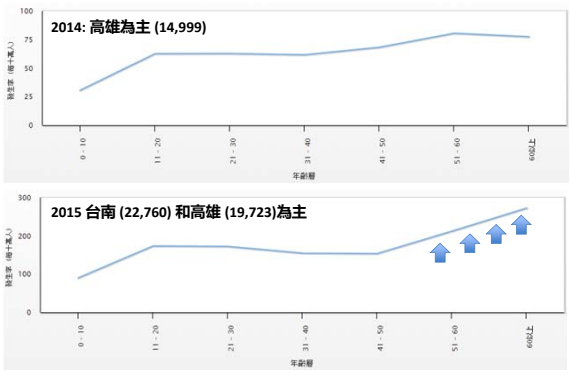

**Figure 2. Age composition of the cases reported in the dengue outbreak in Guangdong in 2014.** Patients aged 16–65 years old accounted for approximately 83.1% of all DF cases, with 65.9% in young age groups (21–55 years old). A main peak appeared in the 21- to 35-year-old group, and a secondary peak appeared in the 41- to 55-year-old group.

*Sci Rep 2015 Nov 23;5:16913*

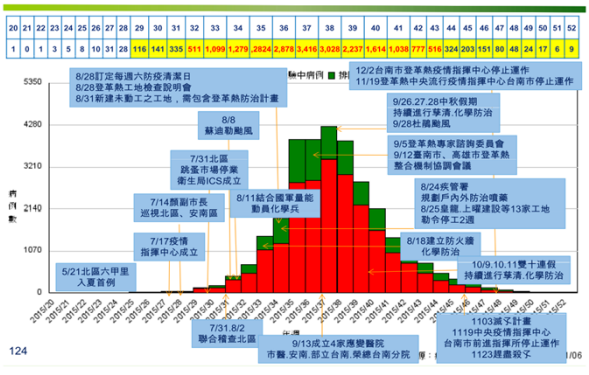
## Tainan City-based Dengue Data


*PLoS ONE 2017;12(11):e0188065*

## 台灣登革熱患者年齡分布

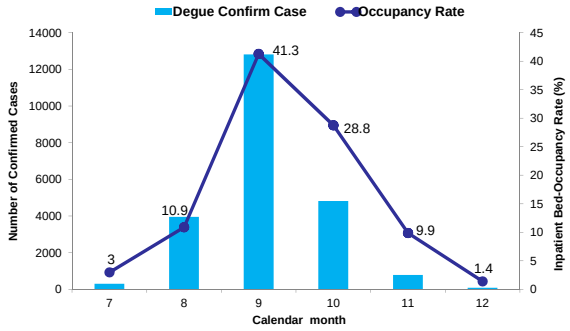



## 2015年入夏以來台南市登革熱趨勢圖

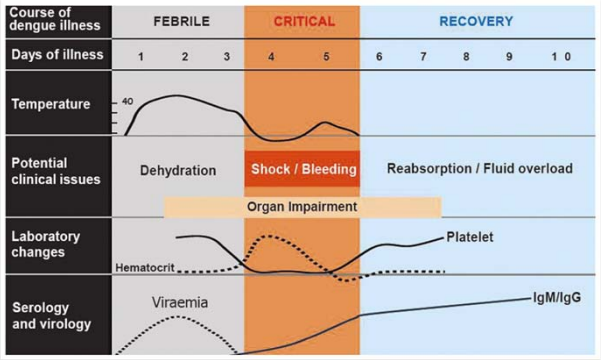



*– 2015年臺南市登革熱防疫作為*

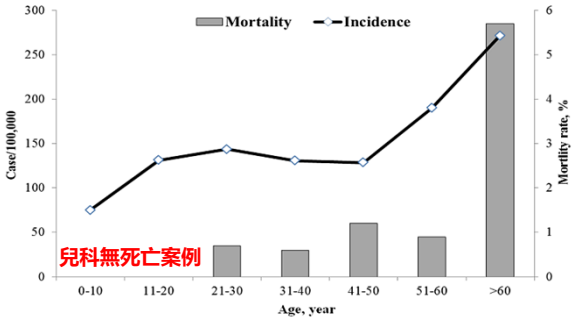
## Inpatient bed-occupancy by dengue cases at NCKUH, 2015




## Natural History of Dengue Fever




## Incidence of DF among different age groups in Tainan and age-related mortality rates of DF, Jan-Nov 2015

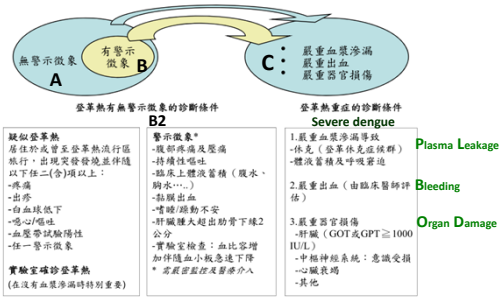



兒科無死亡案例

*- Dr. PL Chen, NCKUH*

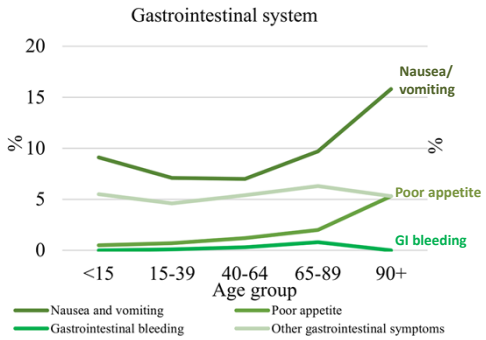
## Skin rash of dengue fever

## 台灣登革熱病例通報定義 (2015.5.1起)
## WHO登革熱病例分類, 2009




**B1: 有潛在疾病因素及特定社經狀況病人，如糖尿病、腎衰竭、慢性溶血疾病、肥胖、懷孕婦女、嬰兒、老人，或具特定社經情況之病人，如獨居或偏遠地區居民**

**Secondary data from the Dengue Disease Reporting System, 2015: 22,777 laboratory-confirmed reported cases**




*PLoS Negl Trop Dis 11(12): e0006091*

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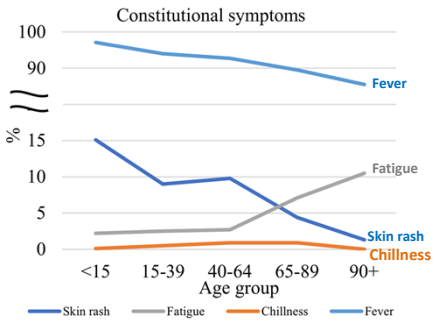


*PLoS Negl Trop Dis 11(12): e0006091*

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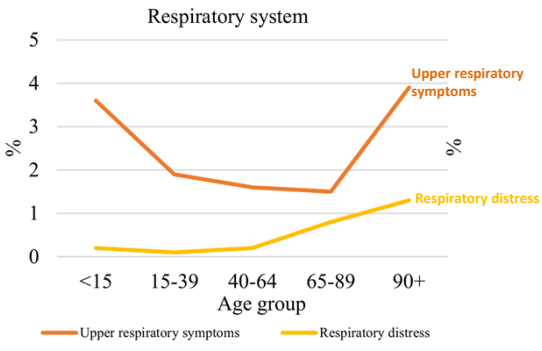


*PLoS Negl Trop Dis 11(12): e0006091*

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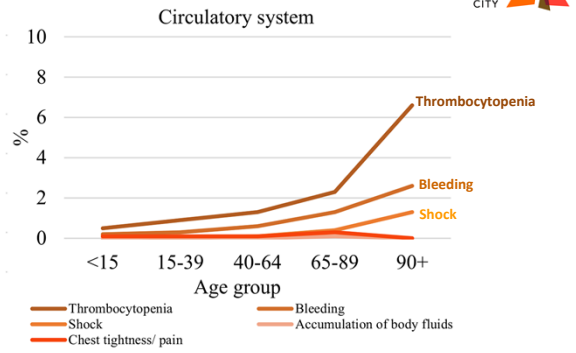


*PLoS Negl Trop Dis 11(12): e0006091*

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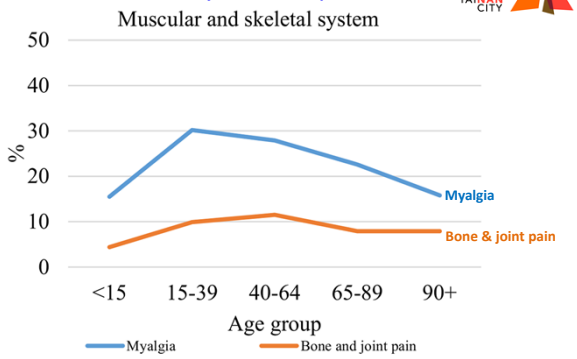


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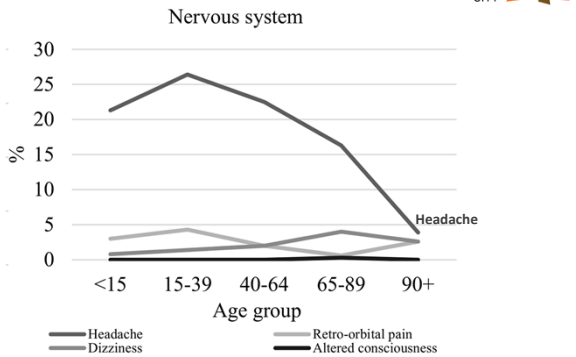
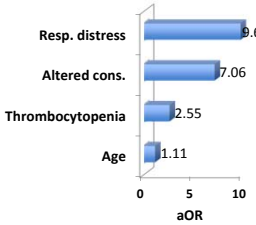



*PLoS Negl Trop Dis 11(12): e0006091*

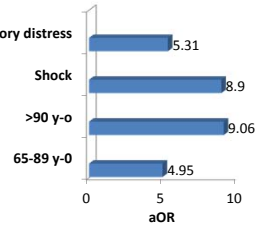
**Secondary data from the Dengue Disease Reporting System, 2015: 22,777 laboratory-confirmed reported cases**

**Factors associated with an increased risk**

**MORTALITY**




**ICU ADMISSION**




**Dengue patients >65 years and those with severe and non-specific signs and symptoms at the time of reporting were at a higher risk of ICU admission and mortality.**

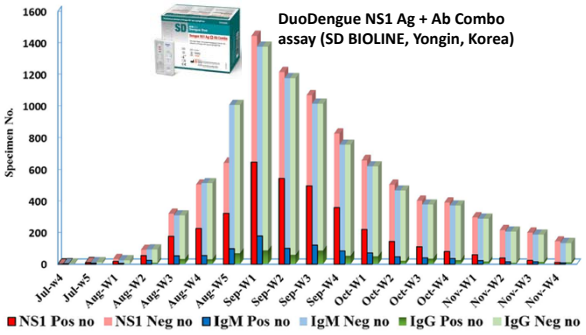
*PLoS Negl Trop Dis 11(12): e0006091*

Secondary data from the Dengue Disease Reporting System, 2015: 22,777 laboratory-confirmed reported cases

- 年紀越大，不典型症狀較多，危急症狀較明顯
  - 隨著年紀越大，初始全身症狀較不明顯 (如：發燒、肌肉痛、頭痛、關節骨頭痛、紅疹、後眼窩痛)
  - 初始警示或危急症狀較明顯 (如：體液蓄積、血小板減少、出血、呼吸窘迫、意識改變)
- 高重症照護需求: 年紀、男性、倦怠、出血、休克、呼吸窘迫、意識改變
- 高死亡風險: 年紀越大、血小板減少、休克、胸痛

*PLoS Negl Trop Dis 11(12): e0006091*

Detection of DENV NS1 antigen and DENV-specific IgM/IgG antibodies at Clinical Virology Laboratory of NCKUH, Jul-Nov 2015




*PLoS Negl Trop Dis 2016;10(10):e0005036*

## Hospital-based Dengue Data

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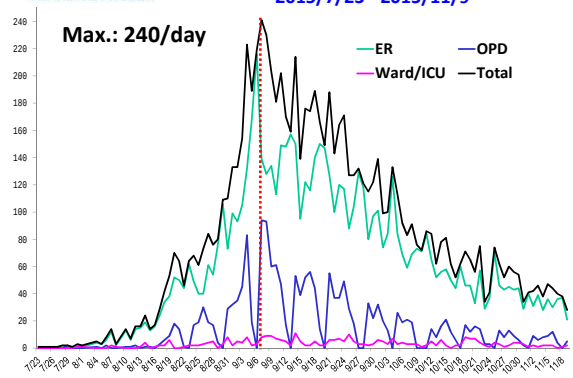
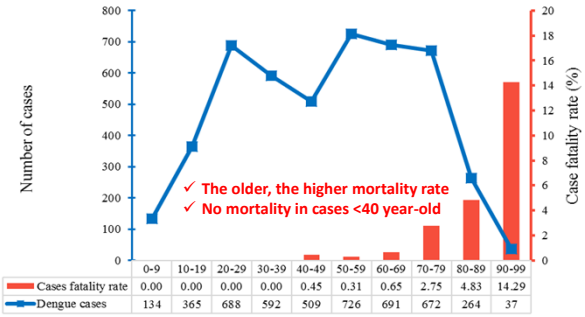
Daily test numbers of dengue virus NS1 antigen 2015/7/23 - 2015/11/9



## Age and fatality rates for 4,678 patients with dengue, 2015




| | 0-9 | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 | 80-89 | 90-99 |
|---|---|---|---|---|---|---|---|---|---|---|
| Cases fatality rate | 0.00 | 0.00 | 0.00 | 0.00 | 0.45 | 0.31 | 0.65 | 2.75 | 4.83 | 14.29 |
| Dengue cases | 134 | 365 | 688 | 592 | 509 | 726 | 691 | 672 | 264 | 37 |

## Comorbidities of 617 Hospitalized Patients with Laboratory-confirmed Dengue

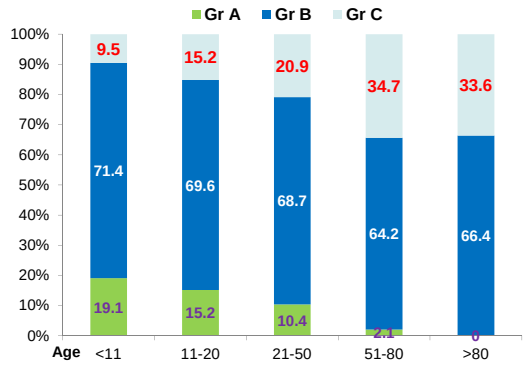
| Comorbidities | N (%) |
|---|---|
| Hypertension | 329 (53.3) |
| Diabetes mellitus | 208 (33.7) |
| Chronic kidney disease | 157 (25.4) |
| End stage renal disease on regular dialysis | 19 (3.1) |
| Cancer (solid tumor) | 104 (12.9) |
| Coronary artery disease | 82 (13.3) |
| Old stroke | 73 (11.8) |
| Peptic ulcer disease | 55 (8.9) |
| Liver cirrhosis | 18 (2.9) |
| Systemic Lupus Erythematosus | 6 (1.0) |
| Leukemia | 2 (0.3) |

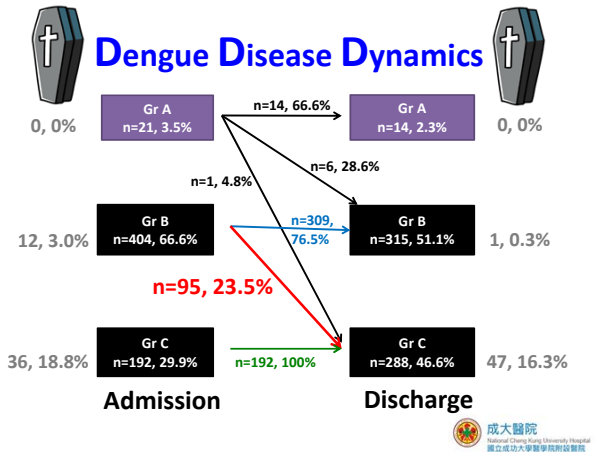
## 617 Hospitalized Patients with Laboratory-confirmed Dengue (2015.07.01-2015.12.31)

| Characteristics | N, (%) or mean ± SD |
|---|---|
| Age, year | 63.8 ± 21.7 |
| Gender, male | 324 (52.5) |
| Comorbidity | 472 (76.5) |
| Warning sings at presentation | 548 (88.8) |
| Severe dengue | 284 (46.0) |
| Acute kidney Injury | 52 (8.4) |
| Sequential bacterial infections | 47 (7.6) |
| Bloodstream infections | 31 (5.0) |
| ICU care | 84 (13.6) |
| Hospital stay, days | 8.6 ± 8.0 |

30-day mortality: 7.8%

## Dengue Severity in Different Age Groups Among Hospitalized Patients with DF



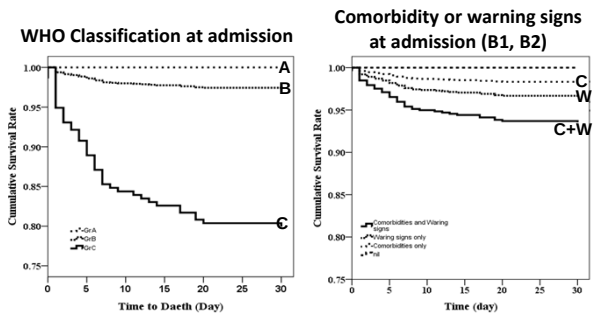



## Risk Factors of Dengue fever Progression

### In Hospitalized Patients: From Gr. B to Gr. C

| Variables | Stationary (n=309) | Progressive (n=95) | Univariate analysis OR (95% CI) | *P* values | Multivariate analysis OR (95% CI) | *P* values |
|---|---|---|---|---|---|---|
| Age; mean±S.D ,years | 61.3±23.2 | 69.6±16.5 | - | <0.001 | 1.01 (0.98-1.03) | 0.13 |
| Male gender | 154 (49.8) | 47 (49.5) | 1.01 (0.8-1.17) | 1.0 | | |
| Waring Sign | 269 (87.1) | 87 (91.6) | 1.62 (0.73-3.59) | 0.28 | | |
| Co-morbidity | 221 (71.5) | 79 (83.2) | 1.97 (1.09-3.55) | 0.023 | | |
| No of Co-morbidity | 2.0±1.9 | 2.9±2.2 | | <0.001 | | |
| **Diabetes mellitus** | 86 (27.8) | 47 (49.5) | 2.54 (1.58-4.07) | <0.001 | **1.91 (1.01-3.64)** | **0.046** |
| **Chronic kidney disease** | 56 (18.1) | 48 (50.5) | 4.6 (2.81-7.57) | <0.001 | **4.4 (2.4-8.28)** | **<0.001** |
| ESRD on regular Dialysis | 4 (1.3) | 3 (3.2) | 2.49 (0.55-11.31) | 0.36 | | |
| Solid tumor | 51(16.5) | 14 (14.7) | 0.87 (0.46-1.66) | 0.75 | | |
| Leukemia | 1 (0.3) | 0 (0) | 1.0 (0.99-1.001) | 1.0 | | |
| Liver cirrhosis | 9 (2.9) | 3 (3.2) | 1.09 (0.29-4.10) | 1.0 | | |
| **CVA** | 27 (8.7) | 22 (23.2) | 3.15 (1.7-5.85) | <0.001 | **2.58 (1.24-5.36)** | **0.01** |
| CAD | 33 (10.73) | 19 (20.0) | 2.09 (1.13-3.88) | 0.02 | | |
| Co-morbidity with Waring Sign | 187 (60.5) | 72 (75.8) | 2.04 (1.21-3.44) | 0.007 | | |
| Obesty | 237 (40.3) | 73 (97.7) | 1.01 (0.59-1.74) | 1.0 | | |

## Survival Analysis of Hospitalized Patients with DF




log-rank test: *P*<0.001

## Risk Factors of 30-day Mortality

### In 617 Hospitalized Patients With Dengue Fever

| Variables | Survivors (n=571) | Non-survivors (n=46) | Univariate analysis OR (95% CI) | *P* values | Multivariate analysis OR (95% CI) | *P* values |
|---|---|---|---|---|---|---|
| **Age**; median (IQR), years | 72 (55-78) | 76 (71-84) | - | <0.001 | **1.05 (1.02-1.09)** | **0.002** |
| Male gender | 304 (93.8) | 20 (6.2) | 1.25 (0.87-1.72) | 0.22 | 1.98 (0.97-3.97) | 0.06 |
| Co-morbidity | 430 (91.1) | 42 (8.9) | 3.44 (1.21-9.77) | 0.011 | 2.92 (0.82-10.42) | 0.1 |
| Hypertension | 303 (53.1) | 26 (56.5) | 1.15 (0.63-2.11) | 0.76 | | |
| Diabetes mellitus | 187 (32.7) | 21 (45.7) | 1.73 (0.94-3.16) | 0.10 | | |
| Chronic kidney disease | 173 (30.3) | 28 (60.8) | 3.58 (1.93-6.64) | <0.001 | 1.57 (0.73-3.39) | 0.25 |
| Malignancy | 91 (15.9) | 13 (28.3) | 2.09 (1.05-4.1) | 0.04 | **2.32 (1.04-5.20)** | **0.04** |
| Liver cirrhosis | 15 (2.6) | 3 (6.5) | 2.59 (0.72-9.28) | 0.14 | | |
| Cerebral vascular accident | 65 (11.4) | 8 (17.4) | 1.64 (0.73-3.67) | 0.23 | | |
| Coronary artery disease | 74 (13.0) | 8 (17.4) | 1.41 (0.64-3.15) | 0.37 | | |
| **Sequential infection** | **35 (6.1)** | **12 (26.1)** | **5.4 (2.58-11.35)** | **<0.001** | **3.35 (1.40-8.03)** | **0.007** |
| **Emergency dialysis** | **19 (3.3)** | **10 (21.7)** | **8.1 (3.5-18.63)** | **<0.001** | **4.04 (1.39-16.63)** | **0.01** |
| **Waring sign presentation** | 479 (83.9) | 45 (97.8) | 8.46 (1.18-63.49) | 0.008 | **8.5 (1.07-67.45)** | **0.04** |
| **Severe Dengue at admission** | 156 (27.3) | 36 (78.3) | 9.58 (4.64-19.76) | <0.001 | **7.51 (3.4-16.63)** | **<0.001** |

Data are given as the numbers (percentages) unless otherwise specified. Ellipses indicate "not available".
OR indicates odds ratio, CI confidence interval,

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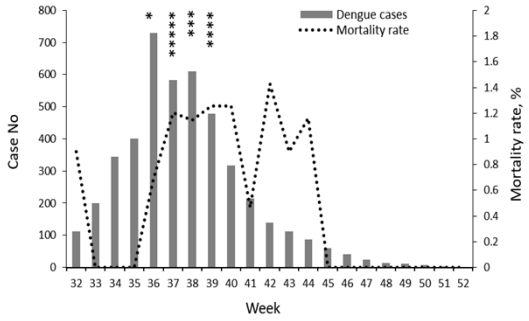
## 13 cardiac arrest events at ED in Tainan dengue outbreak




*Dr. Lee JC, Unpublished data*

## Expanded dengue syndrome: Unusual or atypical manifestations

| System | Unusual or atypical manifestations |
|---|---|
| Neurological | Febrile seizures in young children.<br>Encephalopathy.<br>Encephalitis/aseptic meningitis.<br>Intracranial haemorrhages/thrombosis.<br>Subdural effusions.<br>Mononeuropathies/polyneuropathies/Guillane-Barre Syndrome.<br>Transverse myelitis. |
| Gastrointestinal/hepatic | Hepatitis/fulminant hepatic failure.<br>Acalculous cholecystitis.<br>Acute pancreatitis.<br>Hyperplasia of Peyer's patches.<br>Acute parotitis. |
| Renal | Acute renal failure.<br>Hemolytic uremic syndrome. |
| Cardiac | Conduction abnormalities.<br>Myocarditis.<br>Pericarditis. |

*Trop Med Int Health 2007; 12(9):1087-95*

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## 13 cardiac arrest events at ED in Tainan dengue outbreak

| Serial No. | OHCA | | | | | IHCA | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| Age | 55 | 62 | 69 | 80 | 62 | 45 | 76 | 70 | 76 | 41 | 78 | 74 | 83 |
| Gender | F | M | F | F | M | M | F | M | M | F | F | F | F |
| Latest ER arrival to CPR, hours | | | | | | 1 | 14 | 7 | 4 | 39 | 20 | 22 | 46 |
| Prior ER or OPD visits | Y | N | N | Y | Y | Y | N | N | N | Y | Y | N | N |
| WHO grade on latest ER arrival | C | C | C | C | C | C | B | C | B | A | B | B | B |
| Underlying disease | | | | | | | | | | | | | |
| Charlson's comorbidity index | 5 | 9 | 3 | 8 | 6 | 3 | 6 | 5 | 5 | 1 | 4 | 6 | 9 |
| CNS disease | | | | | • | | | • | | | | | |
| Coronary arterial disease | | • | | • | • | | | • | | | | | • |
| Heart failure | | | | • | | | | | | | | | |
| Hypertension | | | | • | | | • | • | • | | | • | • |
| Liver disease | | | | | | • | | | | | | | |
| Chronic kidney disease | | • | | • | | | • | | | | | • | • |
| Diabetes mellitus | • | • | | | • | | | • | • | | | | |
| Cancer | • | | | | | | | | | | | | |
| Unstable vital signs at the triage | • | • | • | • | • | • | | • | • | | | | |
| Thrombocytopenia at ER | | • | • | | | • | • | • | | | • | • | • |
| Evidence of plasma leakage at ER | • | | | • | | • | • | • | | | • | • | • |

OHCA, out-hospital cardiac arrest; IHCA, in-hospital cardiac arrest at the emergency room; CPR, cardiopulmonary resuscitation; ER, emergency room; OPD, outpatient department; CNS, central nervous system.

*Dr. Lee JC, Unpublished data*

## Expanded dengue syndrome: Unusual or atypical manifestations

| System | Unusual or atypical manifestations |
|---|---|
| Respiratory | Acute respiratory distress syndrome.<br>Pulmonary haemorrhage. |
| Musculoskeletal | Myositis with raised creatine phosphokinase (CPK).<br>Rhabdomyolysis. |
| Lymphoreticular/bone marrow | Infection associated haemophagocytic syndrome.<br>IAHS or Haemophagocytic lymphohistiocytosis (HLH), idiopathic thrombocytopenic purura (ITP).<br>Spontaneous splenic rupture.<br>Lymph node infarction. |
| Eye | Macular haemorrhage.<br>Impaired visual acuity.<br>Optic neuritis. |
| Others | Post-infectious fatigue syndrome, depression, hallucinations, psychosis, alopecia. |

*Trop Med Int Health 2007; 12(9):1087-95*

## Characteristics and initial laboratory data at the onset day of dengue fever (D0) among 4,069 hospitalized patients* in NCKUH, 2015

| Variables | Fatal patients, n=37 | Surviving patients, n=4,032 | P values |
|---|---|---|---|
| Age, years | 74.9±12.0 | 47.8±21.5 | <0.0001 |
| Male gender | 14 (37.8%) | 2039 (50.6%) | 0.12 |
| Days between illness onset and diagnosis | 1 (0-5) | 1 (0-67) | 0.05 |
| Days between illness onset and death | 4 (0.7) | --- | |
| Days between diagnosis and death | 2 (-1-7) | --- | |
| Ever hospitalization after the illness onset | 24 (64.9%) | 534 (13.2%) | <0.0001 |
| Aspartate transaminase (U/L)[a] | 185 (47-1,481) | 35 (17-1,019) | <0.0001 |
| Alanine transaminase (U/L)[b] | 33.5 (10-357) | 16 (10-491) | 0.10 |
| Activated partial thromboplastin time (seconds)[c] | 39.7 (30.9-60.8) | 38 (27.5-93.2) | 0.65 |
| Platelet (x10$^3$/μl)[d] | 113 (19-228) | 166 (5-567) | 0.38 |

Note: Data are expressed as case number (%), mean ± standard deviation, median (range)
[a] 6 records from 6 patients in the fatal group and 529 records from 526 patients in the survivor group were provided at D0.
[b] 16 records from 16 patients in the fatal group and 1,105 records from 1,097 patients in the survivor group were provided at D0.
[c] 7 records from 7 patients in the fatal group and 306 records from 305 patients in the survivor group were provided at D0.
[d] 3 records from 3 patients in the fatal group and 546 records from 542 patients in the survivor group were provided at D0.

***Of 4,069 patients, 0.9% (37) died in one week after illness onset (*i.e.*, early mortality)**

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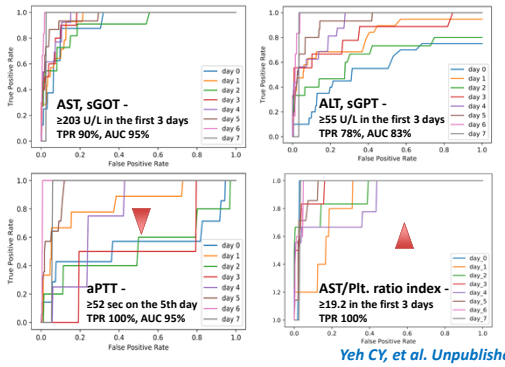
*Yeh CY, et al. Unpublished data*

## Receiver operating characteristic curves of 4 variables in patients with dengue fever within 7 days after illness onset

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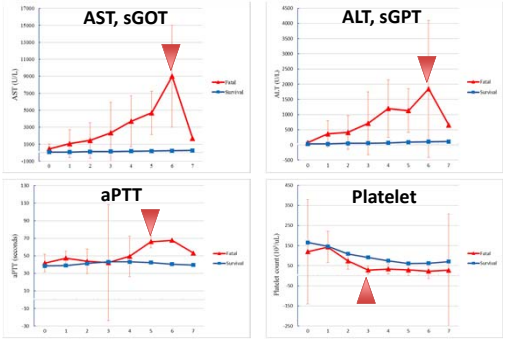
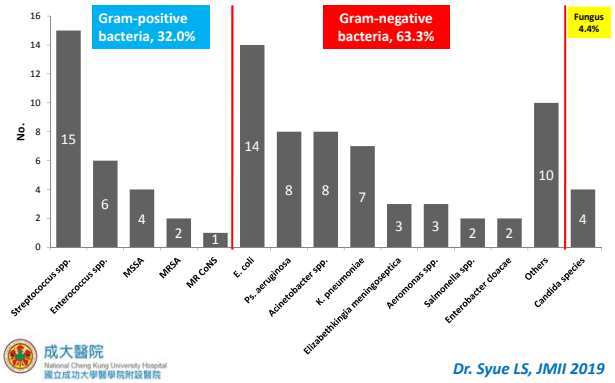
*Yeh CY, et al. Unpublished data*

## Trend variations in 4 lab. variables of fatal and surviving patients with dengue fever within 7 days after illness onset




*Yeh CY, et al. Unpublished data*

## Pathogen distribution of BSIs in DF

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*Dr. Syue LS, JMII 2019*

## Pathogen distribution of Bloodstream Infections in DF

| Pathogens | Isolate number (%) | | | |
|---|---|---|---|---|
| | All isolates n = 90 | Group I n = 38 | Group II n = 34 | Group III n = 18 |
| Gram-positive pathogens | 29 (32.0) | 17 (44.7) | 9 (13.2) | 3 (16.7) |
| *Streptococcus* species | 15 (16.7) [a] | 11 (28.9) | 4 (11.8) | 0 (0) |
| *Enterococcus* species | 6 (6.7) | 2 (5.3) [b] | 1 (2.9) [b] | 3 (16.7) [c] |
| Methicillin-susceptible *Staphylococcus aureus* | 4 (4.4) | 1 (2.6) | 3 (8.8) | 0 (0) |
| Methicillin-susceptible *Staphylococcus epidermidis* | 2 (2.2) | 2 (5.3) | 0 (0) | 0 (0) |
| Methicillin-resistant *Staphylococcus aureus* | 1 (1.1) | 1 (2.6) | 0 (0) | 0 (0) |
| Methicillin-resistant coagulase-negative staphylococci | 1 (1.1) | 0 (0) | 1 (2.9) | 0 (0) |
| Gram-negative pathogens | 57 (63.3) | 21 (55.3) | 23(67.6) | 13 (72.2) |
| *Escherichia coli* | 14 (15.6) | 9 (23.7) | 4 (11.8) | 1 (5.6) |
| *Pseudomonas aeruginosa* | 8 (8.9) | 3 (7.8) | 3 (8.8) | 2 (11.1) |
| *Acinetobacter* species | 8 (8.9) [d] | 3 (7.8) | 3 (8.8) | 2 (11.1) |
| *Klebsiella pneumoniae* | 7 (7.8) | 1 (2.6) | 5 (14.7) | 1 (5.6) |
| *Elizabethkingia meningoseptica* | 3 (3.3) | 0 (0) | 0 (0) | 3 (16.7) |
| *Aeromonas* species | 3 (3.3) [e] | 0 (0) | 3 (8.8) | 0 (0) |
| *Salmonella* species | 2 (2.2) | 0 (0) | 1 (2.9) | 1 (5.6) |
| *Enterobacter cloacae* | 2 (2.2) | 0 (0) | 1 (2.9) | 1 (5.6) |
| Others | 10 (11.1) | 5 (13.2) [f] | 3 (8.8) [g] | 2 (11.1) [h] |
| *Candida* species | 4 (4.4) | 0 (0) | 2 (5.9) | 2 (11.1) |

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## Clinical characteristics and outcomes of 80 hospitalized adults with dengue fever and bloodstream infection (BSI) categorized by the time between admission and BSI onset

| Characteristics | All cases n = 80 | Group I n = 32 | Group II n = 32 | Group II n = 16 | *P* value |
|---|---|---|---|---|---|
| Clinical condition &disease severity | | | | | |
| Admission to BSI, days | 5.8 ± 8.5 | 0.4 ± 0.8 | 4.8 ± 1.2 | 18.4 ± 11.9 | <0.0001 |
| DF onset to BSI [a], days | 7.8 ± 8.7 | 2.3 ± 1.9 | 6.9 ± 2.0 | 20.6 ± 11.7 | <0.0001 |
| Concurrent gastrointestinal bleeding | 32 (40.0) | 15 (46.9) | 14 (43.8) | 3 (18.8) | 0.15 |
| Leukocytosis (≥9,000/mm³) at BSI onset | 32 (40.0) | 11 (34.4) | 12 (37.5) | 9 (56.3) | 0.32 |
| Thrombocytopenia (≤100,000/mm³) at BSI onset | 62 (77.5) | 25 (78.1) | 28 (87.5) | 9 (56.3) | 0.05 |
| Antibiotic usage before BSI | 23 (28.8) | 1 (3.1) | 10 (31.3) | 12 (75.0) | <0.0001 |
| Multidrug-resistant pathogens | 28 (35.0) | 8 (25.0) | 8 (25.0) | 12 (75.0) | 0.001 |
| Inappropriate empirical antibiotic | 35 (43.8) | 14 (43.8) | 10 (31.3) | 11 (68.8) | 0.05 |
| Pitt bacteremia score ≥4 at BSI onset | 30 (37.5) | 13 (40.6) | 12 (37.5) | 5 (31.3) | 0.82 |
| APACH II score while BSI event | 19.6 ± 11.8 | 22.0 ± 12.6 | 19.6 ± 12.3 | 14.8 ± 7.1 | 0.13 |
| Clinical outcomes | | | | | |
| Total length of hospitalization | 17.4 ± 20.6 | 9.1 ± 8.2 | 12.1 ± 8.2 | 44.4 ± 31.3 | <0.0001 |
| Severe dengue | 48 (60.0) | 19 (59.4) | 18 (56.3) | 11 (68.8) | 0.70 |
| Intensive care unit admission | 41 (51.2) | 16 (50.0) | 15 (46.9) | 10 (62.5) | 0.58 |
| Ventilation failure | 27 (33.8) | 10 (31.3) | 10 (31.3) | 7 (43.8) | 0.64 |
| In-hospital mortality | 26 (32.5) | 12 (37.5) | 10 (31.3) | 4 (25.0) | 0.67 |

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Clinical characteristics and outcomes of 80 hospitalized adults with dengue fever and bloodstream infection (BSI) categorized by the time between admission and BSI onset

| Characteristics | All cases n = 80 | Group I n = 32 | Group II n = 32 | Group II n = 16 | *P* value |
|---|---|---|---|---|---|
| Age, years | 73.2 ± 9.4 | 75.6 ± 7.4 | 72.6 ± 9.4 | 69.6 ± 11.7 | 0.10 |
| Male | 41 (51.3) | 15 (46.9) | 19 (59.4) | 7 (43.8) | 0.48 |
| Comorbidities | | | | | |
| Charlson comorbidity index | 2.38 ± 1.99 | 3.13 ± 2.28 | 1.84 ± 1.67 | 1.94 ± 1.53 | 0.02 |
| Hypertension | 59 (73.8) | 28 (87.5) | 20 (62.5) | 11 (68.8) | 0.07 |
| Diabetes mellitus | 41 (51.3) | 18 (56.3) | 13 (40.6) | 10 (62.5) | 0.28 |
| Chronic kidney disease | 21 (26.3) | 9 (28.1) | 9 (28.1) | 3 (18.8) | 0.75 |
| Coronary artery disease | 16 (20) | 6 (18.8) | 7 (21.9) | 3 (18.8) | 0.94 |
| Cerebrovascular disease | 10 (12.5) | 6 (18.8) | 3 (9.4) | 1 (6.3) | 0.37 |
| Malignancy | 16 (20) | 10 (31.3) | 4 (12.5) | 2 (12.5) | 0.12 |

- Group I (BSI onset within 48 hours after admission), Group II (between >48 hours and one week), Group III (more than one week)

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## Risk factors of in-hospital mortality among 80 hospitalized adults with dengue fever and bloodstream infection (BSI)

| Characteristics | All patients, n = 80 | | | Group I and II [a], n = 64 | | |
|---|---|---|---|---|---|---|
| | Surviving n = 54 | Fatal n = 26 | *P* value | Surviving n = 42 | Fatal n = 22 | *P* value |
| Age (mean ± SD), years | 72.5 ± 9.4 | 74.7 ± 9.5 | 0.35 | 73.3 ± 8.7 | 75.8 ± 8.2 | 0.27 |
| Charlson comorbidity index (mean ± SD) | 2.1 ± 2.0 | 3.0 ± 1.8 | 0.07 | 2.2 ± 2.2 | 3.1 ± 1.8 | 0.12 |
| Multidrug-resistant pathogens | 15 (27.8) | 13 (50.0) | 0.05 | 7 (16.7) | 9 (40.9) | 0.03 |
| Inappropriate empirical antibiotic therapy | 19 (35.2) | 16 (61.5) | 0.03 | 12 (28.6) | 12 (54.5) | 0.04 |
| Pitt bacteremia score ≥ 4 at BSI onset | 5 (9.3) | 25 (96.2) | 0.00 | 3 (7.1) | 22 (100) | 0.00 |

SD = standard deviation.

[a] Defined as patients developed BSI within one week after hospital arrival.

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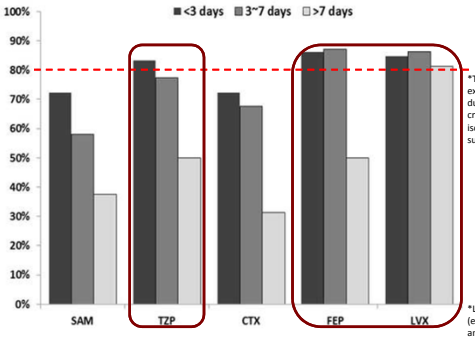
## Susceptibility profile of 83 bacteremic isolates from hospitalized adults with dengue fever




*Three *Moraxella* isolates were excluded for susceptibility tests due to no interpretation criteria and five gram-positive isolates were not available for susceptibility tests.

*Levofloxacin for 78 isolates (excluding 3 *Staphylococcus* and 2 *Streptococcus* isolates)

*Dr. Syue LS, JMII 2019*

## Who will get bloodstream infections?

- Tan Tock Seng Hospital Singapore, concurrent bacteremia in patients with dengue: PBS of ≥4 (aOR 14.73, 95% CI 1.30–167.28)
  - *J Microbiol Immunol Infect 2017;50(3):314-20*
- CMH, risk factors of concurrent bacteremia in patients critically ill with severe dengue: higher CRP levels (aOR: 1.026; 95 % CI 1.008-1.044; P=0.005] and longer APTTs (aOR: 1.034; 95% CI: 1.004-1.065; P=0.027)
  - *J Med Microbiol 2016;65(12):1505-11*
- CKMH KHH, independent risk factors for dengue + bacteremia: acute renal failure (OR 51.45, P = 0.002) and prolonged fever (> 5 days) (OR 26.07, P = 0.017)
  - *Am J Trop Med Hyg 2005;72(2):221-6*

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## Two fatal cases of *Aeromonas dhakensis* bacteremia and necrotizing fasciitis in severe dengue patients

NCKUH x 1
KMCH x 1

D1/2

D3 B/C: *A. dhakensis*



D4

MOF
CVVH
B/T PRBC, Plt, FP

D6

Expired on D8

*J Microbiol Immunol Infect 2018 May 18*
*pii: S1684-1182(18)30108-7*

## ICU-based Dengue Data

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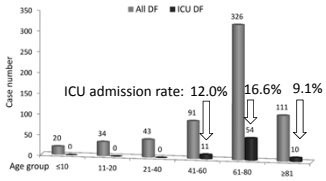
## 75 dengue adults in ICUs

20150701-20151231




- Mean age: 72.3 year-old
- Three major comorbidities: HTN (72.0%); Diabetes mellitus (43.7%); Chronic kidney disease (22.7%)

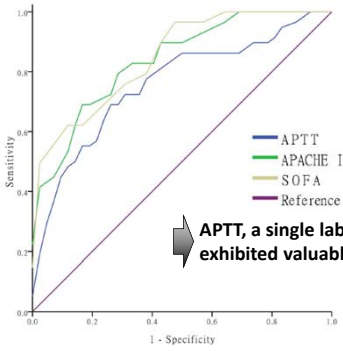
- In-hospital case fatality rate 41.3%
  - Independent risk factors:
    - ① cardiac arrest before ICU admission (HR: 6.26)
    - ② initial prolonged APTT (>48 sec; HR: 3.91)
    - ③ acute kidney injury at ICU admission* (HR:2.48)

*AKI (defined by KDIGO clinical practice guidelines) in the first 24 h after ICU admission.

*PLoS Negl Trop Dis 2017; 11(1): e0005270*

## Epidemiology/Laboratory-based Dengue Data

## ROC curves of 3 continuous variables in predicting in-hospital fatality of dengue adults in ICUs




Area under ROC curves

0.76
0.84 } P=.27
0.85 } P=.16

APTT, a single laboratory parameter, exhibited valuable prognostic significance.

*PLoS Negl Trop Dis 2017; 11(1): e0005270*

## Suboptimal diagnostic performance of dengue NS-1 antigen rapid test during non-endemic periods in southern Taiwan

- 1,262 non-duplicated patients tested by NS1 antigen: 16 (1.27%) positive results
- Exclusion of 6 patients with recent travel to dengue-endemic countries, false-positive rate: 70.0% (7/10)

Table. Clinical diagnosis of seven patients with false-positive NS1 antigen rapid test results.

| No. | Age/Sex | Acute illness | Chronic underlying diseases |
|---|---|---|---|
| 1 | 37y/M | Septic shock and Lemierre's syndrome with *Fusobacteirum necrophorum* bacteremia | Renal lithiasis |
| 2 | 58y/M | Septic shock, spondylodiskitis and psoas muscle abscess with MRSA[a] bacteremia | Spinal cord injury, end-stage renal disease, gallstones |
| 3 | 10m/F | Roseolla infantum | nil |
| 4 | 19y/M | Acute suppurative tonsillitis | nil |
| 5 | 78y/F | Acute ischemic stroke | Adrenal insufficiency, peptic ulcer disease |
| 6 | 65y/M | Scrub typhus | Hypertension, atrial fibrillation |
| 7 | 85y/F | Influenza A(H3) with septic shock | Atrial fibrillation |

[a]Methicillin-resistant *Staphylococcus aureus*

*SD BIOLINE Dengue NS1 Ag rapid test (Standard Diagnostics, Yongin, Korea).
*January 01, 2016 - December 31, 2017

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*Cong-Tat Cia, Wen-Chien Ko. JMII (Accepted)*

## Prolonged persistence of IgM against dengue virus detected by commonly used commercial assays

- Prospectively investigated 44 adults with anti-DENV IgM in the 2015 dengue epidemic in Tainan: 17 symptomatic, 27 asymptomatic
- Anti-DENV IgM: ELISA tests from Standard Diagnostic (SD) and Focus Diagnostic
- Rapid IgM test: SD BIOLINE Dengue Duo rapid dengue tests

| | Initial | | 6 months | | 12 months | |
|---|---|---|---|---|---|---|
| **ELISA tests** | **SD** | **Focus** | **SD** | **Focus** | **SD** | **Focus** |
| **All cases** | 44/44<br>100% | 40/44<br>91% | 31/44<br>71% | 6/44<br>14% | 18/39<br>46% | 3/39<br>8% |
| **Symptomatic** | 17/17<br>100% | 16/17<br>94% | 11/17<br>65% | 1/17<br>6% | 7/15<br>47% | 1/15<br>7% |
| **Asymptomatic** | 27/27<br>100% | 24/27<br>89% | 20/27<br>74% | 5/27<br>19% | 11/24<br>46% | 2/14<br>8% |
| **Anti-DENV IgM, rapid tests** | **86.4%** | | **68.2%** | | **35.9%** | |

*BMC Infect Dis (2018) 18:156*

## Summary

- **Multiple chronic diseases and comorbid conditions in elderly dengue patients**
- **Elderly dengue patients are likely to present atypical symptoms**
- **Clinical deterioration (Gr. B ➡ C): underlying diabetes mellitus, chronic kidney disease, or old stroke**
- **Prognostic factors**
  - **hospitalized adults with DF: increased age, underlying cancer, sequential bacterial infection, emergent dialysis, warning signs or severe dengue at presentation**
  - **severe dengue in ICUs: cardiac arrest before admission, acute respiratory or renal failure at admission, and APTT >48 seconds**