

1 **Full title:** Causes of death among hospitalized adults with dengue fever  
2 in Tainan, 2015: emphasis on cardiac events and bacterial infections

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4 **Short title:** Causes of death among hospitalized adults with dengue fever

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26

27 **Keyword:** dengue fever, fatality, mortality, bacterial infection, bacteremia, cardiac

28 arrest, Taiwan

## 29 **Abstract**

30 **Introduction.** The 2015 dengue outbreak in southern Taiwan caused substantial  
31 mortality rates in the elderly. We analyzed here the causes of death among adults with  
32 dengue.

33 **Methods.** The retrospective study was conducted at a medical center in Tainan from  
34 the 1<sup>st</sup> of August to 31<sup>th</sup> of December in the year 2015. The detection of the dengue  
35 NS1 antigen IgM or viral RNA in patients' blood were used to diagnose dengue.  
36 Clinical courses and causes of death were retrieved from chart reviews by two  
37 intensivists.

38 **Results.** There were 4,488 cases of dengue diagnosed in the study hospital, and these  
39 cases had an in-hospital case fatality rate of 1.34% (60 cases). Of these, the mean age  
40 was 73 years and gender did not predict outcome. Twenty-eight (46.7%) cases died of  
41 severe dengue, and 29 (48.3%) deaths were possibly caused by dengue-related  
42 complications, which were mostly secondary infections (24 cases). Most of the  
43 families of fatal case (70%) signed do-not-resuscitate (DNR) orders prior to the  
44 patients' death. When the dengue epidemic peaked, 13 cardiac arrest events, including  
45 out-of-hospital (5 events) and in-hospital (8) cardiac arrests at the emergency  
46 department, occurred within four weeks of the dengue epidemic. Notably, in half (7)  
47 of these cases, the patients did not search for medical aid prior to experiencing cardiac  
48 arrest. Of the 40 cases that had early death (occurring within one week after  
49 hospitalization), 60% died of severe dengue. In contrast, 50% of the 20 deaths that  
50 occurred later than one week after hospitalization were related to hospital-acquired  
51 infections, mainly pneumonia.

52 **Conclusion.** The elderly that experience dengue fever may die of severe dengue early

53 or die of secondary infections later. Cardiac arrests can also occur unpredictably at the  
54 first aids, which highlight the need of professional and patient education regarding the  
55 danger signs that are related to severe dengue in an epidemic setting.

## 56 **Author summary**

57       The 2015 dengue outbreak in Tainan City caused substantial deaths among the  
58 elderly. The main causes of death were severe dengue and its complications. We here  
59 highlight the deaths caused by heart complications of dengue that the elderly has  
60 underlying cardiovascular comorbidities is more prone to be involved. The  
61 presentations of heart complications vary, ranging from arrhythmia to myocarditis and  
62 to unexpected cardiac arrest. Clinicians should carefully evaluate and monitor the  
63 heart function of patients with severe dengue and provide timing intervention.  
64 Secondary infections or healthcare-associated infections may occur throughout the  
65 whole hospitalized course. They were also the leading causes of death during the late  
66 or recovery phase of dengue in the study. Judicious application of antimicrobial  
67 agents and early elimination of infection source may be beneficial. Overall, the  
68 substantial deaths during this outbreak may be related to low public awareness of  
69 dengue, emergency department overclouding, and lack of clinical experience.  
70 Professional and public education regarding the danger signs that are related to severe  
71 dengue is necessary in an epidemic setting.

## 72 **Introduction**

73 Dengue is a mosquito-borne viral disease that affects humans and is emerging as  
74 a major threat to public health throughout the tropics and subtropics [1, 2]. Dengue  
75 affects children primarily in hyper-endemic areas [3] where epidemiological studies  
76 have shown the susceptible age group moved toward older children and adults [4].  
77 Taiwan is not a hyperendemic area, but dengue outbreaks develop almost every year  
78 [5, 6]. Dengue predominantly affects adults in Taiwan. The highest prevalence rate is  
79 among people in their sixties [6]. During 2015, a large-scale dengue outbreak, which  
80 was caused by the dengue virus serotype 2, occurred in Tainan City [7] and a total of  
81 22,777 dengue cases were confirmed [8]. Among these, 2%-3% had severe diseases  
82 or complications that required intensive care [9, 10]. However, with the increased  
83 utilization of intensive care units, the hospital stays for severe dengue patients were  
84 prolonged and more invasive devices were used. Healthcare-associated infections thus  
85 became unavoidable during the recovery phase.

86 Atypical presentations of dengue in the elderly are not uncommon [11] and make  
87 early diagnoses difficult. With multiple comorbidities complicating the clinical course  
88 of dengue, the elderly has more severe presentations and a higher mortality rate than  
89 children and young adults during this outbreak [12]. To know their cause of deaths  
90 may alarm early symptoms and signs of life-threatening conditions to clinicians.  
91 However, this information was limited in the literature. A two-year review in  
92 Malaysia has discussed deaths that were directly caused by dengue [13]. The causes  
93 of death stratified by the pathophysiology of dengue fever include dengue shock  
94 syndrome, severe bleeding, and severe organ involvement. Two case series that  
95 include seven and ten cases, respectively, mention deaths that were related to the  
96 complications other than dengue [14, 15]. Other studies that have paramedical points

97 of view, discuss how these factors involve clinicians, patients, and the medical  
98 system, will lead to dengue death [16, 17]. The present study aimed to analyze the  
99 causes of death among dengue patients that were cared at a medical center in 2015.

## 100 **Methods**

### 101 **Case inclusion**

102 The study was conducted at the National Cheng Kung University Hospital  
103 (NCKUH), a medical center in southern Taiwan, between August 1<sup>st</sup> and December  
104 31<sup>th</sup> in the year 2015. Cases of dengue were identified from the dengue notification in  
105 the Infection Control Center, NCKUH. The diagnosis of dengue fever was established  
106 by the documentation of dengue NS1 antigen (Bioline Dengue NS1 Ag kit, Standard  
107 Diagnostics Inc., Korea), dengue IgM (Bioline Dengue Duo kit, Standard Diagnostics  
108 Inc., Korea), or dengue virus RNA (TIB Molbiol, Lightmix kit, Roche Applied  
109 Science, Berlin, Germany) in the sera or blood of the patients. The study protocol was  
110 approved by the Institutional Review Board at NCKUH (A-ER-104-386) and  
111 informed consents were waived. The study was funded by Ministry of Health and  
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113 had no role in study design, data collection and analysis, decision to publish, or  
114 preparation of the manuscript.

115

### 116 **Definitions**

117 Cardiac arrest events at the emergency department (ED) included out-hospital  
118 cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA). The weekly mortality  
119 rate was determined as the ratio of fatal case number and the number of newly  
120 diagnosed cases of dengue fever during the indicated week. Typical presentations of  
121 dengue fever included fever with two of the following symptoms or signs:  
122 nausea/vomiting, rash, aches/pains, positive tourniquet test, leucopenia, or any of  
123 warning signs [18]. If the initial manifestations of dengue did not fulfil the above  
124 criteria of the typical presentations, these cases were considered to be atypical. The

125 severity of dengue fever was graded using the WHO guidelines issued in 2009 [18].  
126 Group A includes those without warning signs, Group B those with warning signs, co-  
127 existing complicated conditions, or special social circumstances, and Group C  
128 includes those with the signs of severe plasma leakage, severe hemorrhages, or severe  
129 organ impairment. Plasma leakage was supported by a hematocrit change of more  
130 than 20% or the presence of pleural effusion or ascites. Unstable vital signs indicate  
131 the presence of hypotension (systolic pressure less than 90 mmHg or mean pressure  
132 less than 65 mmHg), impending respiratory failure, or altered mental status. The age-  
133 modified Charlson's index was used to evaluate comorbidity status [19]. Days of  
134 hospitalization here were included days of ED stay.

135 Organ failure associated with dengue fever was defined as the dysfunction of the  
136 cardiovascular system, respiratory system, nervous system, liver, or kidney after  
137 dengue onset. Cardiovascular failure was defined as the patients having a mean blood  
138 pressure of less than 65 mmHg, the need of inotropic agents to maintain blood  
139 pressure, or low cardiac output signs. Respiratory failure was defined as a  $\text{PaO}_2/\text{FiO}_2$   
140 ratio of less than 300 [20] or  $\text{PaCO}_2$  more than 50 mmHg [21], with or without  
141 increased breathing effort. Nervous system failure was characterized as the patient  
142 having a Glasgow Coma scale score of less than 8 [22]. Serum bilirubin level of more  
143 than 2 mg/dl was regarded as liver failure [20]. The KDIGO criteria were applied to  
144 define renal failure, *i.e.*, an increase of serum creatinine levels of more than twice the  
145 baseline level or more than 4 mg/dl, urine output of less than 0.3 ml/kg/hour over 24  
146 hours, or anuria for 12 hours [23]. Multiorgan failure was defined as the presence of  
147 failure of more than two organ systems.

148

149 **Causes of death**

150 Cause of death in the cases of dengue fever was evaluated by two intensivists  
151 with complete training in infectious diseases. The causes of death were categorized  
152 into three groups. Death was considered to be related to “severe dengue” if the patient  
153 died of severe plasma leakage, major bleeding, or organ failures. If the patient died of  
154 organ failures but we were unable to attribute this death solely to severe dengue, the  
155 death was classified as “possibly dengue related”. If there were other clinical diseases  
156 that inevitably lead to death, the cause of death was classified as “other”.

157

### 158 **Data acquisition**

159 All parameters including demographic information, underlying disease, status of  
160 organ system dysfunction, date and cause of death, dengue onset, date of hospital  
161 visiting, and timing of the do-not-resuscitation (DNR) order, were obtained and  
162 calculated from electronic medical records.

163

### 164 **Statistical methods**

165 To analyze the causes of death, patients were further stratified into deaths within  
166 one week of hospitalization and deaths after one week. Chi-squared or Fisher exact  
167 tests were used to compare categorical variables between groups. Continuous  
168 variables were compared using a Student’s t-test. All data were processed using SPSS  
169 (20th edition, IBM). A *P* value of less than 0.05 is denoted as significant.

## 170 **Result**

171 During the study period, there were 4,488 hospitalized cases of serologically  
172 documented dengue in NCKUH, Tainan. Among these patients, 60 died with a crude  
173 in-hospital mortality rate of 1.34%, and 40 (66.7%) died within seven days of  
174 hospitalization. The mortality rate reached a peak of 1.57% during the 40th week and  
175 the case number reached its peak in the 36th week of 2015.

176 The mean age of patients in fatal cases was 73 years and the major underlying  
177 medical illnesses were hypertension (32 cases, 53.3%), diabetes mellitus (30, 50%),  
178 and chronic kidney disease (20, 33.3%), as shown in Table 1.

179

**Table 1.** Clinical characteristics of 60 fatal cases of dengue fever.

Parameters	Case No. (%)
Age (mean $\pm$ standard deviation), years	73.4 $\pm$ 12.4
Underlying disease	
Hypertension	32 (53.3)
Diabetes mellitus	30 (50.0)
Chronic kidney disease	20 (33.3)
Cancer	16 (26.7)
Coronary arterial disease	15 (25.0)
Neurological disease	12 (20.0)
Rheumatic disease	8 (13.3)
Congestive heart failure	7 (11.7)
Chronic hepatitis	7 (11.7)
Liver cirrhosis	4 (6.7)
Chronic obstructive pulmonary disease or asthma	4 (6.7)
Chronic renal replacement therapy	2 (3.3)
Recent chemotherapy	2 (3.3)

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Neurological disease indicates one or more of old stroke, dementia, parkinsonism, or multiple sclerosis.

180

181       As for the causes of death, 46.7% (28 cases) died of severe dengue, and 65%  
182 (39) of the deaths were possibly related to dengue (Table 2). Of the later, a substantial  
183 proportion (40%, 24 cases) died of secondary infections. Two (3.3%) deaths were  
184 related to acute renal failure, and two (3.3%) died of respiratory failure without  
185 advanced airway management. A patient that refused interventional procedures died  
186 of massive gastrointestinal bleeding, which occurred while the patient had a platelet  
187 count of  $94 \times 10^9/L$  during the 22<sup>nd</sup> day of hospitalization. Three patients died from a  
188 brain tumor, medication suffocation, and a traffic accident that caused a skull bone  
189 fracture and intracranial hemorrhage and were coincident with dengue fever,  
190 respectively.

191

**Table 2.** Clinical characteristics of the deaths of adults with dengue fever occurring  $\leq 1$  week and  $>1$  week after their hospitalization.

Variables	Death after hospitalization		<i>P</i> value
	$\leq 1$ week, n=40	$>1$ week, n=20	
Age (mean $\pm$ standard deviation), years	73.1 $\pm$ 13.4	75.2 $\pm$ 10.5	0.52
Male gender	17 (42.5)	13 (65)	0.17
Causes of death			
Severe dengue	24 (60)	4 (20)	0.03
Intracranial hemorrhage	2 (5)	3 (15)	0.32
Cardiac events	5 (12.5)	0 (0)	0.16
Possibly dengue-related	14 (35)	15 (75)	0.003
Secondary infections	14 (35)	10 (50)	0.58
Bacteremia	6 (15)	0 (0)	0.17
Candidemia	2 (5)	1 (5)	1
Pneumonia	5 (12.5)	8 (40)	0.02
Pneumonia and bacteremia	1 (2.5)	0 (0)	1
Necrotizing fasciitis	0 (0)	1 (5)	0.33
Renal failure and its complication	0 (0)	2 (10)	0.11
Respiratory failure	0 (0)	2 (10)	0.11
Lower gastrointestinal bleeding	0 (0)	1 (5)	0.33
Others	2 (5)	1 (5)	1
Do-not-resuscitate	24 (60)	18 (90)	0.02
Cardiac arrest events at ED	13 (32.5)	0 (0)	0.03

ED, emergency department

192

193         The death causes were compared between those dying within one week and those  
194 after one week of hospitalization (Table 2). For the former, the primary causes of  
195 death were severe dengue (24 cases, 60%) and secondary infection (14, 35%). Of the  
196 24 deaths caused by severe dengue, five (12.5%) died from cardiac events that

197 included fatal arrhythmia, myocarditis, and refractory heart failure. Among those that  
198 died after one week of hospitalization, the major causes of death were secondary  
199 infections (10 cases, 50%), renal failure (2, 10%), and respiratory failure (2, 10%).  
200 There were four (20%) cases in which the patients died from severe dengue. Of these,  
201 three (15%) died from intracranial hemorrhage, which developed during the critical  
202 phase of dengue. Candidemia can occur either early (within one week, two cases) or  
203 late (after one week, one case) during hospitalization. In contrast, among the seven  
204 fatal cases in which death was caused by bacteremia, all of these deaths occurred  
205 during the first week.

206 The mortality rate and the number of new cases and cardiac arrest events at the  
207 ED by week are shown in Figure 1. Of note, 13 cardiac arrest events occurred  
208 between the 36th and 39th week of 2015, also when the dengue outbreak peaked.  
209 Among the cases that had cardiac arrest, five occurred out-of-hospital cardiac arrest  
210 (OHCA) and eight had in-hospital cardiac arrest (IHCA) while staying at the ED  
211 (Table 3).

212

213 **Figure 1. Weekly notified dengue cases in the study hospital and early mortality**  
214 **rates.** The case number of newly diagnosed dengue patients came to peak in the  
215 Week 36 while the early mortality rate (*i.e.*, death within the first week of  
216 hospitalization). peaked in the Week 40. Cardiac arrest events occurred mainly in  
217 Week 36-39 when the outbreak was in full swing. An asterisk (\*) indicates a cardiac  
218 arrest event at the emergency department.

**Table 3.** Characteristics of 13 cardiac arrest events at the emergency department.

Serial No.	OHCA					IHCA							
	1	2	3	4	5	6	7	8	9	10	11	12	13
Age	62	80	62	55	69	83	76	74	76	70	78	45	41
Gender	M	F	M	F	F	F	F	F	M	M	F	M	F
Latest ED arrival to CPR, hours						46	14	22	4	7	20	1	39
Prior ED or OPD visits	No	Yes	Yes	Yes	No	No	No	No	No	No	Yes	Yes	Yes
WHO grade on latest ED arrival	C	C	C	C	C	B	B	B	B	C	B	C	A
Underlying disease													
Charlson's comorbidity index	9	8	6	5	3	9	6	6	5	5	4	3	1
Central nervous system disease			•							•			
Coronary arterial disease	•	•	•			•				•			
Heart failure		•											
Hypertension		•				•	•	•	•	•			
Liver disease												•	
Chronic kidney disease	•	•				•	•	•					
Diabetes mellitus	•		•	•					•	•			
Cancer				•									
Unstable vital signs at the triage	•	•	•	•	•				•	•		•	
Thrombocytopenia at ED	•				•	•	•	•		•	•	•	
Evidence of plasma leakage at ED		•		•		•	•	•		•	•	•	
Interval from onset to death, days	ND	4	ND	6	0	6	1	3	0	2	5	0	5

CPR, cardiopulmonary resuscitation; ED, emergency department; IHCA, in-hospital cardiac arrest at the ED; ND: no data; OHCA, out-of-hospital cardiac arrest; OPD, outpatient department.

219

220 The intervals between ED arrival and the IHCA event varied, ranging between  
221 one and 46 hours. The estimated interval between dengue onset and death ranged  
222 between 0 and 6 days. Ages in these cases ranged between 41 and 83 years and the  
223 Charlson's index ranged between 1 and 9. Of these 13 cases, 7 cases did not search  
224 for medical aid prior to the events, and 12 cases presented to the ED with severe  
225 dengue (WHO Grade B or C). The exception was a case of WHO Grade A disease  
226 that died soon after the onset of upper back pain with diffuse ST-T elevation (Figure  
227 2) in electrocardiography records at the ED. This is shown as case 13 in Table 3.

228

229 **Figure 2. Electrocardiography record from a patient with dengue fever that was**  
230 **dying of myocarditis.** The diagnosis of myocarditis was suggested by the diffuse ST-  
231 T elevation (case 13 in Table 3).

232

233 Of the 60 fatal cases, 70% (42) signed do-not-resuscitate (DNR) orders prior to  
234 their death (Table 4), and two thirds (28 cases) of DNR decisions were made within  
235 one week after their hospital arrival. Of note, DNR was requested in six cases without  
236 organ failure, twelve with failure of one organ system, and eight with failure of two  
237 organ systems

**Table 4.** Number of organ failures in the 42 fatal cases of dengue fever at the time of the do-not-resuscitate (DNR) signature.

Parameters	Case No. (%)
No organ failure	6 (14.3)
Failure of one organ system	12 (28.6)
Respiratory failure	5 (11.9)
Renal failure requiring renal replacement therapy	4 (9.5)
Cardiovascular failure	2 (4.8)
Central nervous system (CNS) failure	1 (2.4)
Failure of two organ systems	8 (19.0)
Renal and respiratory failure	3 (7.1)
CNS and respiratory failure	3 (7.1)
Cardiovascular and respiratory failure	1 (2.4)
CNS and renal failure	1 (2.4)
Multiorgan failure	16 (38.1)

## 238 **Discussion**

239       The 2015 dengue outbreak in southern Taiwan came to its peak in early  
240 September. The mortality rate of patients included in this study reached its peak  
241 during Week 40. Of note, the majority of the sudden death events, including OHCA  
242 and IHCA at the ED, occurred within the first four weeks of the dengue outbreak.  
243 This is likely related to the following: first, public awareness of dengue was low  
244 during the early phase of the epidemic and less than one half (6) of the 13 patients that  
245 experienced cardiac arrest sought medical care before their death. Early medical care  
246 could be life-saving before dengue deteriorated [13-15]. Second, ED overclouding  
247 may be associated with increased mortality rates and morbidity [24, 25], and the role  
248 of patient diversion [24, 26] and the short stay ward at the ED [27] during large  
249 outbreaks of infectious diseases is mentioned. With the implementation of a patient  
250 diversion program in Tainan, and dengue rapid screening clinics in the study hospital,  
251 the ED patient burden was correspondingly decreased, which may facilitate optimal  
252 initial care for the elderly that have severe dengue. Third, a lack of clinical experience  
253 in the ED professional staff may delay the timely diagnosis and appropriate care for  
254 severe diseases. A recent study found that case management training can improve  
255 dengue outcomes [28] and protocolized care may accelerate the transformation of  
256 knowledge [29] and help inexperienced healthcare providers.

257       Dengue in Taiwan often involves the elderly [6], for which the diagnosis of  
258 dengue may be challenging because of atypical presentations [5, 30]. The febrile  
259 elderly with leucopenia has been referred to as a trigger for diagnostic laboratory tests  
260 for dengue fever [31]. The clinical symptoms and signs that are presumably linked to  
261 underlying comorbidities in the elderly can further delay the diagnosis of dengue.  
262 More than half of our patients had atypical presentation during their initial medical

263 visits, and the diagnosis of infection with the dengue virus was delayed in eight cases.  
264 Thus, to achieve the goal of early diagnosis, clinical suspicion of dengue should not  
265 be limited to the typical dengue fever “criteria” in endemic settings.

266 In our series, five OHCA and eight IHCA cases that had atypical presentation at  
267 the ED had a fulminant course. Not all fatal dengue cases received optimal intensive  
268 care in the ED before their death. Thrombocytopenia was not observed in five cases,  
269 and five had no evidence of plasma leakage, contradictory to severe manifestations of  
270 dengue fever [18]. Closely laboratory test and vital sign monitoring may be necessary  
271 in patients really needed intensive care. Another potentially fatal complication of  
272 dengue fever is pericardiomycarditis, which is illustrated by sudden collapse, diffuse  
273 ST-T elevation in electrocardiograms (Figure 2), and elevated serum cardiac enzymes,  
274 but without thrombocytopenia or plasma leakage.

275 The overall mortality rate of hospitalized patients with dengue fever in the study  
276 hospital was 1.3%. Multiple factors, such as increased age or epidemic serotype 2  
277 dengue virus, may contribute to the substantial mortality rate in our study. One  
278 potential contributing sociocultural factor is the DNR signature during hospitalization  
279 in up to 70% of fatal cases. Through advances in organ support, those with severe  
280 dengue may have a greater chance to survive, but DNR orders precludes the intensive  
281 care provided by healthcare workers. In Taiwan, old age is the main factor in signing  
282 DNR orders in critically ill patients [32, 33]. A study in Taiwan revealed that patients  
283 with renal failure had the highest percentage of signed DNR orders [34]. Furthermore,  
284 aspects of Taiwanese culture caused many to refuse tracheostomy [35]. We observed  
285 that dengue patients with DNR orders and without organ failure were older than those  
286 with organ failures, although the difference was not significant. However, their  
287 prognosis may remain poor even without a DNR order under advanced medical

288 support.

289 To further analyze the causes of death, more than half of the early deaths (*i.e.*,  
290 deaths within one week of hospitalization) were related to severe dengue with either  
291 plasma leakage or major bleeding. However, there were three cases in which the  
292 patients experienced rapid organ failure without evidence of plasma leakage and  
293 major bleeding. In contrast, the two main causes of death that occurred after one week  
294 of hospitalization were healthcare-associated bacterial infections and organ  
295 dysfunction that was related to severe dengue. Identifying secondary infections  
296 among hospitalized dengue patients is critical during dengue epidemics. The primary  
297 pathogens that caused bacteremia in dengue patients were *Staphylococcus aureus*,  
298 *Streptococcus* species, and *Enterobacteriaceae* [36]. Old age, comorbidities, severe  
299 disease with gastrointestinal bleeding, prolonged activated prothrombin time, and  
300 acute renal failure were recognized as risk factors for concurrent bacteremia [37-39].  
301 Laboratory parameters, such as leukocyte count [38], serum C-reactive protein [39],  
302 and procalcitonin [40], may be useful to differentiate those with concurrent  
303 bloodstream infections from those that had only dengue virus infection alone.

304 One unique finding in the present study is that cardiac events were associated  
305 with dengue virus infection. Before their death, five patients suffered cardiac events,  
306 including heart failure with cardiogenic shock or pulmonary edema, fatal arrhythmia,  
307 and fulminant myocarditis. In the literature, the disease spectrum for cardiac  
308 involvement in dengue patients was wide and ranged from subclinical functional  
309 myocardial impairment to fulminant myocarditis [41, 42]. Fluid resuscitation may  
310 predispose patients with impaired cardiac function to pulmonary edema, and  
311 arrhythmias may be induced when plasma leakage or renal function impairment was  
312 ongoing. Patients with risk factors, such as old age, underlying cardiovascular disease,

313 abnormal electrocardiogram findings, elevated cardiac enzymes, and shock  
314 unresponsive to fluid resuscitation, warrant further evaluation by cardiac specialists  
315 [43].

316 Our study has several limitations. First, this study was conducted at a single  
317 medical center in southern Taiwan, which provided care for more than half of the  
318 critical patients from Tainan City during the 2015 dengue epidemic. Second, the data  
319 were collected retrospectively, and certain important parameters, such as the time of  
320 disease onset and detailed symptoms and signs, cannot be obtained from medical  
321 records. Third, the causes of death were clinically categorized and cannot be verified  
322 by autopsy. However, the study results were recorded by two experienced intensivists  
323 who had the Taiwan board of infection disease specialization.

324 In conclusion, elderly patients with severe dengue are at risk of fatal cardiac  
325 events and secondary infections. Absence of medical care among one half of adults  
326 with cardiac arrest reveals the importance of health education for the public during  
327 dengue epidemics.

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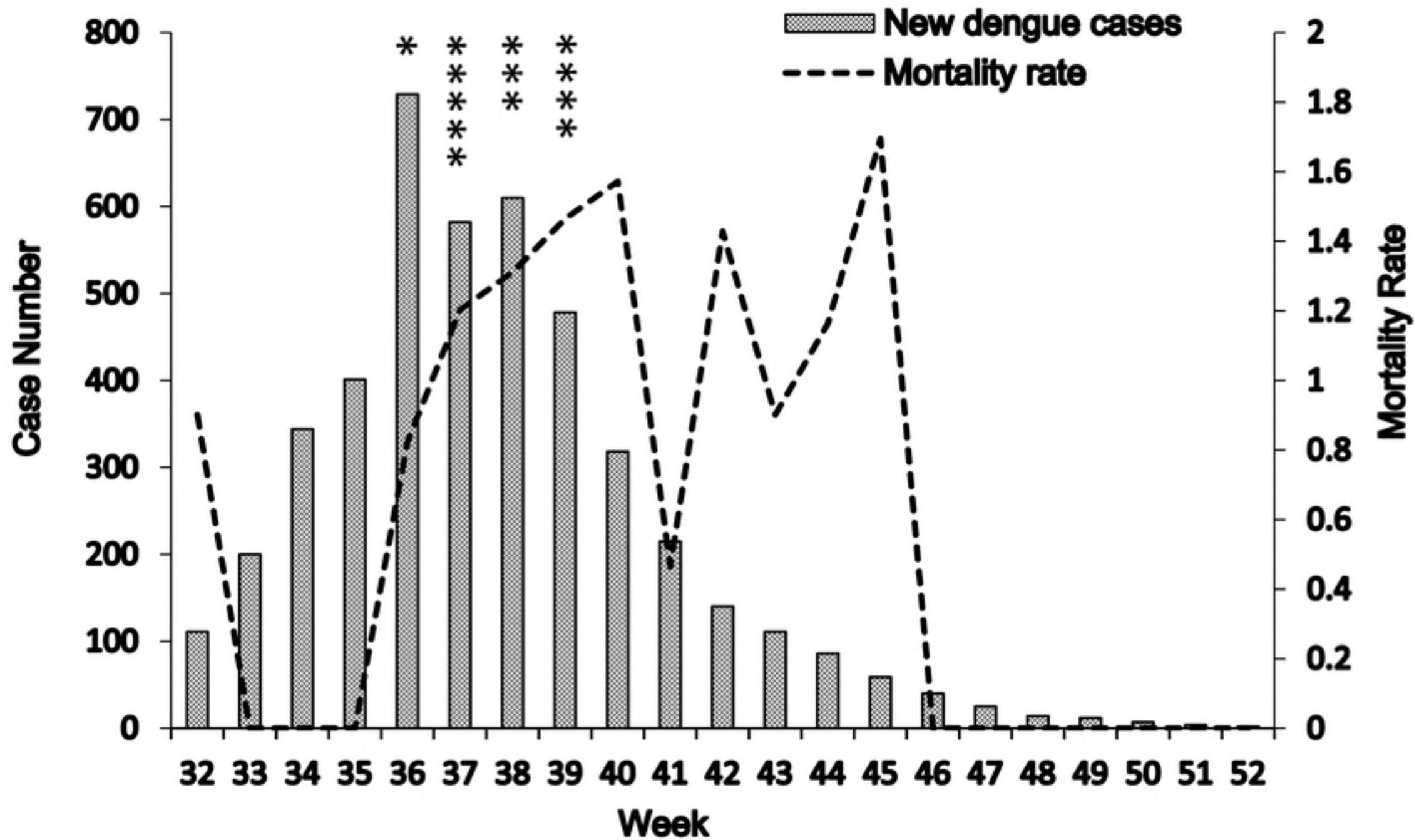
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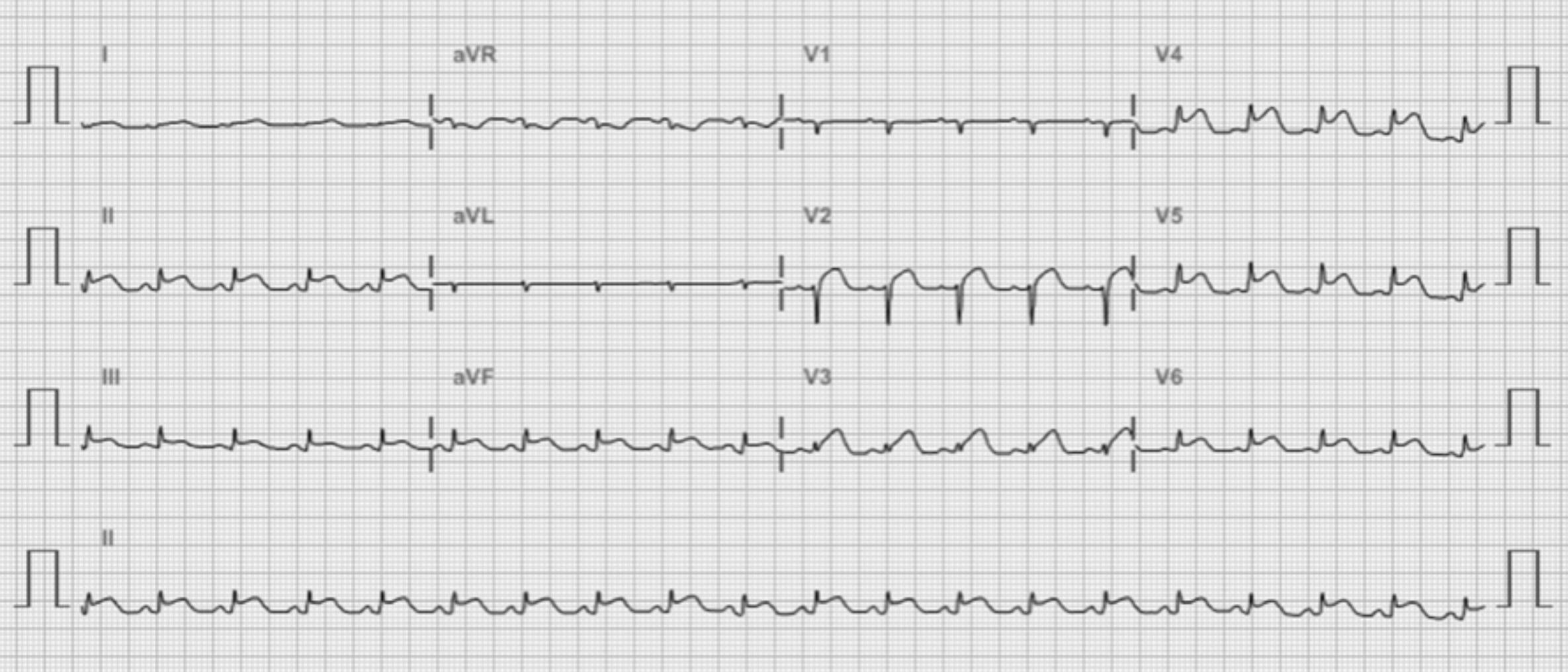
455 **Supporting information**

456 **S1 File. The data base of the 60 fatal cases in 2015 dengue outbreak in Tainan.**

457 **S1 Checklist. STROBE Checklist**



Figure



Figure