CLINICAL AND ETIOLOGICAL DIAGNOSES OF FEBRILE ILLNESS IN PEDIATRICS IN INDONESIA

D. Puspitasari[1], M.H. Gasem[2], E. Tjitra[3], B. Alisjahbana[4], M.M.D.E.A.H. Hapsari[2], A. Alam[4], N.M. Pelupessy[5], I. Savitri[6], I.M.G.D.L. Utama[7], D. Lokida[8], P.M. Tauran[8], H. Kosasih[8], S. Siddiqui[9], M. Karyana[3,8]

[1] Soetomo Hospital, Surabaya, Indonesia , [2]Kariadi Hospital, Semarang, Indonesia, [3]NIHRD, Jakarta, Indonesia, [4]Hasan Sadikin Hospital, Bandung, Indonesia, [5]Wahidin Soedirohusodo Hospital, Makassar, Indonesia, [6]Sardjito Hospital, Yogyakarta, Indonesia, [7]Sanglah Hospital, Denpasar, Indonesia, [8]INA RESPOND, Jakarta, Indonesia, [9]NIAID-NIH, Bethesda, Maryland

BACKGROUND

Febrile illness accounts for approximately 20-25% of hospitalizations in Indonesia, where fever is usually linked to infectious etiologies. Due to non-specific clinical manifestations and limited diagnostic capacity, the etiologies of fever often remain undiagnosed. Several studies have been implemented to study specific pathogens, but no large scale study to identify causes of febrile illness has been conducted. Indonesia Research Partnership on Infectious Diseases (INA-RESPOND) has currently been conducting a study to document etiologies of acute fever among patients who require hospitalization (AFIRE).

METHOD

AFIRE has been conducted at 8 sites (RS Cipto Mangunkusumo and RS Penyakit Infeksi Sulianti Saroso, Jakarta, RS Hasan Sadikin Bandung, RS Kariadi, Semarang, RS Sardjito, Yogyakarta, RS Soetomo, Surabaya, RS Sanglah, Bali, and RS Wahidin Sudirohusodo, Makassar) in Indonesia since 2013. The two sites from Jakarta started the enrollment at the end of the year, and consequently they are not included in this analysis. Children aged 1-18 years with fever ≥38°C and no history of hospitalization in the last 3 months were enrolled into the study within 24 hours after their presentation at the hospitals. Demographic, clinical, and hematology data were obtained; acute, convalescent, and 3-month-after-enrollment specimens were collected. Compulsory blood culture was performed right after enrollment using blood taken from two arms. Other diagnostic tests such as dengue NS1 antigen, dengue IgM/IgG, salmonella IgM, respiratory specimen culture and smear, influenza rapid test, urine culture, and feces microscopic test were performed based on the requests from the attending clinicians.

RESULTS

Figure 1: Study Sites and Enrolled Subjects

510 - Bandung (68)
560 - Semarang (73)
550 - Makassar (25)
570 - Surabaya (47)
580 - Yogyakarta (46)
520 - Denpasar (40)

Table 1: Demography, clinical characteristics, and laboratory findings

Demographics characteristics	Count (%)	Hematology results	Count (%)
Gender		Hemoglobin	
Male	161 (53.8)	Severe anemia	2 (0.7)
Age		Moderate anemia	44 (14.7)
1 -5 year	93 (31.1)	Mild anemia	37 (12.4)
5 - 11 year	138 (46.2)	Normal	216 (72.2)
12 -17 year	68 (22.7)	Leukocyte	
Fever information		Leukopenia	96 (32.1)
Duration of fever before hospitalization		Leukositosis	57 (19.1)
1-3 days	91 (31.9)	Normal	146 (48.8)
4-6 days	127 (44.6)	Platelet	
7-10 days	43 (15.1)	Severe thrombocytopenia (< 50.000/µl)	19 (6.4)
11-14 days	24 (8.4)	Moderate thrombocytopenia (50-99.000/µl)	53 (17.8)
Onset of fever		Mild thrombocytopenia (100-149.000/µl)	48 (16.1)
Abrupt	212 (70.9)	Thrombocytosis (>500.000/µl)	3 (1.0)
Gradual	87 (29.1)	Normal (150-500.000/µl)	175 (58.7)
Type of fever		Hospitalization information	
Continuous	198 (66.2)	Duration of hospitalization (day)	
Remittent	55 (18.4)	Mean (range)	6 (1-54)
Intermittent	46 (15.4)	ICU stay (day)	
Temperature		Median (range)	5 (3-48)
Mean (range)	38.8 (38.0 - 41.2)	Antibiotic	
Signs and symptoms		Antibiotic given prior to hospitalization	
Fever	295 (98.7)	Yes	109 (36.5)
Vomiting	157 (52.5)	Amoxicillin	45 (41.3)
Nausea	139 (46.5)	Cotrimoxazole	8 (7.3)
Cough	135 (45.2)	Cefixime	5 (4.5)
Anorexia	124 (41.5)	Others	51 (46.8)
Lethargy	95 (31.8)	Clinical output	
Headache	87 (29.1)	Cured	164 (56.9)
Runny nose	73 (24.4)	Cured with sequele	66 (22.9)
Abdominal pain	68 (22.7)	Improved	49 (17.0)
Diarrhea	56 (18.7)	Unchanged	5 (1.7)
Arthralgia	54 (18.1)	Death	4 (1.4)
Myalgia	53 (4.0)		

Table 2: Etiological diagnoses confirmed by methods

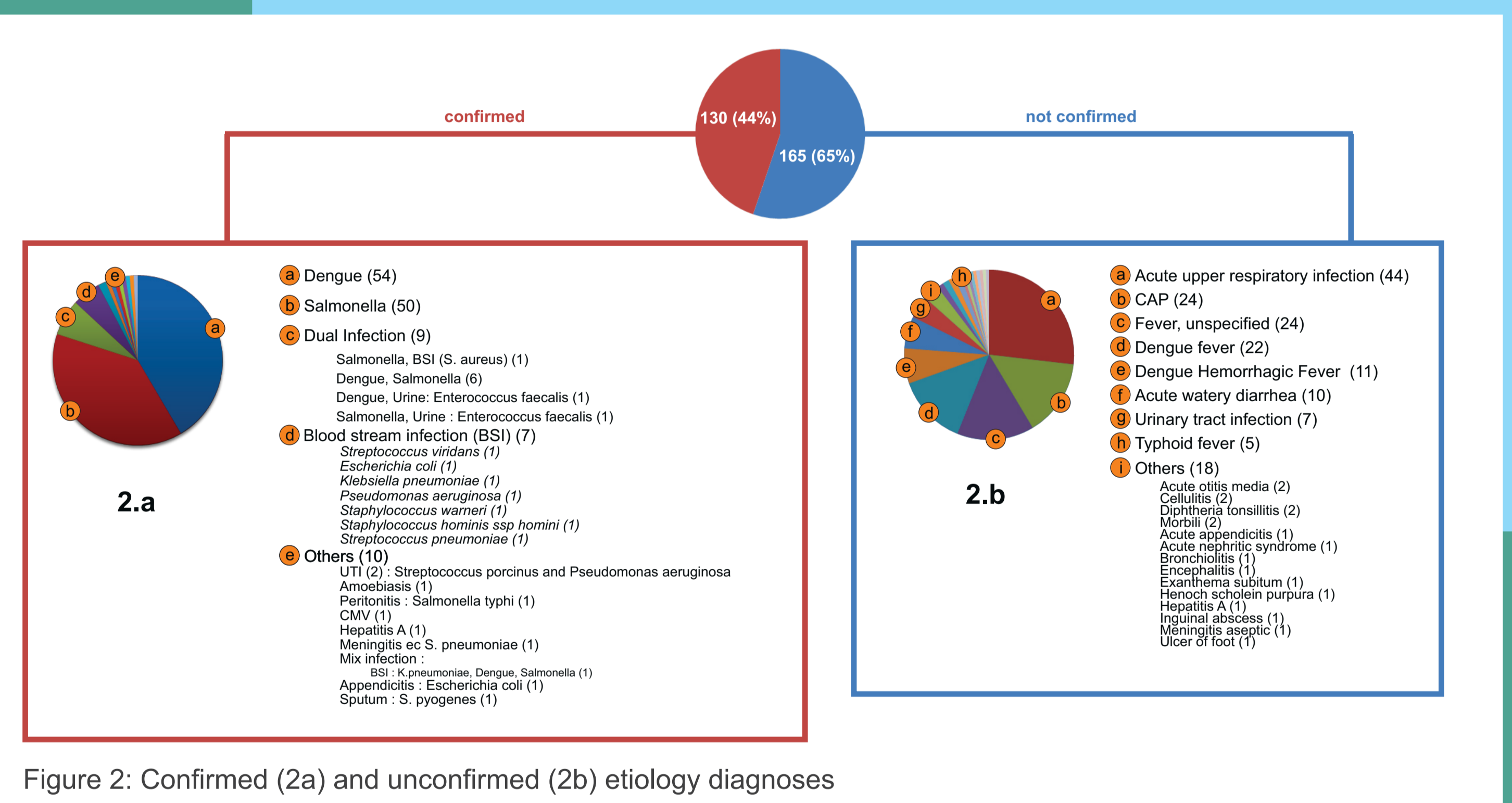|	
Number of subject 299	
Etiological diagnosis confirmed : 134 (44.8%)	
Confirmed etiological diagnosis by methods :	
Blood culture only	18 (6%)
Blood culture and serology	17 (5.7%)
Serology only	80 (26.8%)
Antigen	11 (3.7%)
Other	8 (2.7%)

Figure 2: Confirmed (2a) and unconfirmed (2b) etiology diagnoses

Table 3: Characteristics of deceased subjects

Subject	Signs and symptoms	Clinical diagnosis	Etiological diagnosis	Comorbidity	Cause of death
1.1 yo, female	Fever, cough, runny nose, shortness of breath	CAP, Sepsis	Not confirmed	Congenital malformation of heart, Down syndrome, Underweight	Respiratory distress
17.5 yo, male	Chills, fever, headache, cough, shortness of breath, nausea, epigastric pain, arthralgia	CAP, Sepsis	Salmonella	Severe protein energy malnutrition	Sepsis
7 yo, female	Anorexia, cough, nause, vomiting	HIV	Not confirmed	Malnutrition	HIV
1.2 yo, male	Fever, cough, runny nose, shortness of breath, diarrhea	CAP	Not confirmed	Ventricular septal defect, malnutrition	Respiratory distress

CONCLUCIONS

Dengue and salmonella are the most frequent etiologies of fever. Cultures improved diagnostics by 6%. However, etiologies remained unknown in 48.2% subjects

ACKNOWLEDGEMENT

INA RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE