

SUPPLEMENTAL TABLE

Summary of published epidemiology studies on rickettsial diseases in Southeast Asian countries within the past 15 years (1999–2014)*

Author, year (reference)	Location	Population studied	Overall	Prevalence			Mixed infections	Diagnostic methods and criteria used
				<i>Rickettsia typhi</i>	<i>Orientia tsutsugamushi</i>	SFGR		
Kasper and others, 2012 ⁹⁸	Multiple sites in Phnom Penh and surroundings (50-km radius), Cambodia	9,997 patients referred to site clinics with acute undifferentiated febrile illness	–	261/1946 (13.4%); [†] 56/261 (21.5%) seroconversion	133/1906 (7.0%); [†] 35/133 (26.3%) seroconversion	146/1,263 [‡] (11.6%); [†] 21/146 (14.4%) seroconversion	–	qPCR, paired serum samples for IgG; 1. Seroconversion; 2. ≥ 4 -fold increase in paired serum titers
Richards and others, 2003 ³⁰	Gag Island, Irian Jaya, Indonesia	55 rural asymptomatic patients from a larger cohort screened for malaria and filariasis	–	1/48 (2.1%) by IFA; 1/50 (2.0%) by ELISA	5/53 (9.4%)	5/48 (10.4%) by IFA; 10/49 (20.4%) by ELISA	–	IFA, [§] ELISA, [†] single serum sample; 1. Any seroreactivity
Gasem and others, 2009 ⁹⁹	Semarang, central Java, Indonesia	137 patients ≥ 5 years of age with acute undifferentiated fever presenting to two primary healthcare centers and a tertiary hospital	9/137 (7%)	9/137 (7%); an additional 9/137 (7%) had inconclusive results	None	None	3/13 (23%) patients with leptospirosis had increased <i>R. typhi</i> titers	IFA, paired serum samples; 1. Single titer IgG $\geq 1:256$ and IgM $\geq 1:64$; 2. Seroconversion; 3. ≥ 4 fold increase in paired serum titers
Phongmany and others, 2006 ⁶³	Vientiane, Laos	427 adult patients ≥ 15 years of age with non-malarial fever	115/427 (26.9%)	41/427 (9.6%)	63/427 (14.8%)	11/427 (2.6%); 8 <i>R. helvetica</i> <i>Rickettsia</i> AT1; 1 <i>R. felis</i> ; 1 <i>R. conorii</i> Indian strain	–	IFA, paired serum samples; cross absorption tests; 1. Single titer IgG $\geq 1:128$ and IgM $\geq 1:64$; 2. Seroconversion; 3. ≥ 4 fold increase in paired serum titers
Syhavong and others, 2010 ⁴⁹	Vientiane City and surroundings, Laos	392 patients admitted to a hospital with acute hepatitis	28/382 (7.3%)	14/382 (3.7%)	8/382 (2.1%)	6/382 (1.6%); SFGR species not tested	2 had scrub typhus and leptospirosis and 2 had SFGR and leptospirosis	IFA, paired serum samples; 1. Single titer IgG $\geq 1:128$ and IgM $\geq 1:64$; 2. Seroconversion; 3. ≥ 4 fold increase in paired serum titers
Vallee and others, 2010 ²⁵	Vientiane City and surroundings, Laos	2,002 asymptomatic adults ≥ 35 years of age	–	20.6% (95% CI = 17.4–23.8%)	20.3% (95% CI = 18.1–22.5%)	–	4% had antibodies against scrub and murine typhus	IgG ELISA

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Author, year (reference)	Location	Population studied	Overall	Prevalence			SFG	Mixed infections	Diagnostic methods and criteria used
				<i>Rickettsia typhi</i>	<i>Orientia tsutsugamushi</i>				
Mayxay and others, 2013 ¹⁰⁰	Luang Namtha (northwestern) and Salavan Province (southeastern), Laos	1,938 patients (799, 41%, with a diagnosis) with acute undifferentiated fever presenting to site hospitals	¶	10/799 (1%)#	122/799 (15%)#	**	26 had JEV and scrub typhus co-infections; 10 had dengue and scrub typhus co-infections	Cultures, IFA, paired serum samples, PCR; 1. Single titer IgG or IgM ≥ 1:400	
Tay and others, 1999 ²⁴	Slim River, Malaysia	300 asymptomatic rubber estate workers	198/300 (66.0%)	3/300 (1.0%)	23/300 (7.7%)	120/300 (40.0%); SFG species not tested	An additional 52/300 (17.3%) had mixed rickettsial seropositivity (see reference)	IIP (TT118 used for SFG), single serum sample; 1. Single titer IgG and/or IgM titers ≥ 1:50	
Sagin and others, 2000 ¹⁰¹	Upper Rejang River, Sarawak, Malaysia	261 asymptomatic villagers from 5 Orang Ulu (interior tribe) villages	25/261 (9.6%) by Weil-Felix; 11/261# (4.2%) by IIP	1/261 (0.4%)††	4/261 (1.5%)††	7/261 (2.7%);†† SFG species not tested	2 had seropositivity to mixed rickettsial species	Weil-Felix tests, IIP (TT118 used for SFG?); 1. OX19 or OXK titer ≥ 1:32; 2. Single titer IgG and/or IgM > 1:100	
Tay and others, 2000 ²¹	8 localities (Semenyih, Bandar Tenggara, Bukit Panchor, Slim River, Cheroh, Ketengah Jaya, Selangau, Nabawan) throughout eastern Malaysia and peninsula Malaysia	1,596 patients with febrile illness who presented at health centers	821/1,596 (51.4%)	58/1596 (3.6%)	68/1,596 (4.3%)	198/1596 (12.4%); SFG species not tested	An additional 497/1596 (31.1%) had mixed rickettsial seropositivity (see reference)	IIP (TT118 used for SFG), single acute-phase serum sample; 1. Single titer IgG and/or IgM ≥ 1:50	
Tay and others, 2002 ²³	Slim River, Malaysia	48 patients with febrile illness who presented at health center. Most were rubber estate workers	44/48 (91.7%)‡	1/48 (2.1%)	12/48 (25.0%)	40/48 (83.3%); SFG species not tested	Not reported	Culture (cell culture and animal passage), IFA, IIP (TT118 used for SFG), PCR, single acute-phase serum sample; 1. Single titer IgG and/or IgM titers ≥ 1:50 for IFA and IIP	
Tay and others, 2003 ²²	Kuala Lumpur, Malaysia	240 asymptomatic blood donors and 292 febrile patients admitted to Kuala Lumpur Hospital	35/240 (14.6%) blood donors; 189/292 (64.7%) febrile patients	22/240 (9.2%) blood donors; 67/292 (22.9%) febrile patients	13/240 (5.4%) blood donors; 127/292 (42.5%) febrile patients	4/240 (1.7%) blood donors; 34/292 (11.6%) febrile patients; SFG species not tested	See reference	IIP (TT118 used for SFG), single serum sample; 1. Single titer IgG and/or IgM titers ≥ 1:50	

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Author, year (reference)	Location	Population studied	Overall	Prevalence			SFGR	Mixed infections	Diagnostic methods and criteria used
				<i>Rickettsia typhi</i>	<i>Orientia tsutsugamushi</i>				
Pradutkanchana and others, 2003 ¹⁰²	Hat Yai, Songkhla Province, Thailand	180 pediatric patients with acute fever post-floods	2/180 (1.1%)	0/180 (0%)	2/180 (1.1%)	0/180 (0%)		IFA (TT118 used for SFGR), single or paired serum samples; 1. ≥ 4 fold increase in paired sera titers; 2. Single titer $\geq 1:400$	
Parola and others, 2003 ³	Sangkhlaburi District, Kanchanaburi Province, Thailand (Thailand-Myanmar border)	46 patients ≥ 20 years of age with acute undifferentiated fever, with suspected rickettsioses (multi-test Djip-S- Ticks positive spot sample results)	15/46 (33%)	4/46 (8.7%)	3/46 (6.5%)	8/46 (17.4%); 5 <i>R. Helvetica</i> ; 2 <i>R. conorii</i> Indian strain; 1 <i>R. felis</i>		IFA (panel of 13 rickettsial antigens), paired serum samples, cross-absorption tests for SFGR; 1. Single titer IgG $\geq 1:128$ and/ or IgM $\geq 1:64$ for <i>R. conorii</i> ; 2. Single titer IgG $\geq 1:64$ and/or IgM $\geq 1:32$ for other rickettsiae	
Leelaramee and others, 2004 ¹⁰³	10 community-based hospitals throughout Thailand	1,137 patients who presented to outpatients department with acute undifferentiated fevers	–	65/1,137 (5.3%)	91/1,137 (7.5%)	–		Weil-Felix, IFA, IIP, paired serum samples; 1. ≥ 4 fold increase in antibody titer with Weil-Felix; 2. Increase in titer $\geq 1:200$ if IFA or IIP; 3. Single titer $\geq 1:400$	

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Author, year (reference)	Location	Population studied	Prevalence				Diagnosed methods and criteria used	
			Overall	<i>Rickettsia typhi</i>	<i>Orientia tsutsugamushi</i>	SFGR		Mixed infections
Sutinont, 2006 ²⁷	Multiple hospitals (3 in northeastern Nakhon Rachasima, Loei, Bureem Provinces; 1 in southern Chumphon Province; 1 central: Ratchaburi Province) throughout Thailand	845 patients with acute undifferentiated fever who presented to study site hospitals (malaria and clinically obvious dengue infections excluded)	158/854 (18.6%)	15/845 (1.8%)	135/845 (16.0%)	8/845 (0.9%); All <i>R. helvetica</i> infections	37 patients had leptospira and rickettsial co-infections	MIA (IFA) (<i>R. helvetica</i> , <i>R. felis</i> , <i>R. japonica</i> , <i>R. honei</i> used for SFGR) paired serum samples, cross-adsorption tests for SFGR using <i>R. helvetica</i> and <i>R. honei</i> antigens; 1. ≥ 4 fold increase in paired serum titers; 2. Single titer $\geq 1:400$ for murine and scrub typhus; 3. IgG $\geq 1:64$ and IgM $\geq 1:32$ for SFGR
Ellis and others, 2006 ¹⁰⁴	Sangkhlaburi District, Kanchanaburi Province, Thailand (Thailand–Myanmar border)	613 adult inpatients and outpatients with acute febrile illness	36/613 (5.9%)	9/613 (1.5%)	7/613 (1.1%)	20/613 (3.3%); SFGR species not tested	4/36 (11.1%) had dual rickettsial infections	IFA (not specified for SFGR), paired serum samples (patients with single serum samples excluded); 1. IgG $\geq 1:64$ and/or IgM $\geq 1:32$ for acute-phase or convalescent-phase specimens
Suputtamongkol and others, 2009 ²⁸	Multiple hospitals (4 in northeastern, 1 in southern and 1 in central) throughout Thailand	1,663 patients with acute undifferentiated fever who presented to site hospitals	–	28/1,663 (1.7%)	268/1,663 (16.1%)	Not specifically tested by primary analysis	–	PCR, IFA, paired serum samples; 1. ≥ 4 fold increase in paired serum titers; 2. Single titer $\geq 1:400$; 3. Stable paired titer $\geq 1:200$
			10/178 (5.6%)	0/178 (0.0%)	10/178 (5.6%)	0/178 (0.0%)	–	

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Author, year (reference)	Location	Population studied	Prevalence			Diagnostic methods and criteria used		
			Overall	<i>Rickettsia typhi</i>	<i>Orientia tsutsugamushi</i>		SFGR	Mixed infections
Thitvichianlert and others, 2009 ²⁶	21 provincial army hospitals (7 in central, 4 in northeastern, 5 in northern, 5 in southern) throughout Thailand	178 patients ≥ 15 years of age with acute undifferentiated fever						Dot-ELISA for IgG/IgM for <i>O. tsutsugamushi</i> , IFA (<i>R. honei</i> TT-118 used for SFGR), paired serum samples; 1. Single titer ≥ 1:400 for IFA
McGready and others, 2010 ⁴	Maela refugee camp, Thailand (Thailand–Myanmar border)	203 pregnant women (having 211 diagnoses) attending antenatal clinics with undifferentiated fevers	26/211 (12.3%)	14/211 (6.6%)	11/211 (5.2%)	Not tested	1/211 (0.05%) had murine and scrub typhus; 5/51 (9.8%) with malaria had <i>Rickettsia</i> co-infection	PCR, cultures from buffy coat, IFA, paired serum samples; 1. Positive PCR result; 2. Culture isolation of <i>Rickettsia</i> spp.; 3. ≥ 4 fold increase in paired serum titers
Camer and others, ¹⁰⁵ 2003 ¹⁰⁵	Manila, Luzon and northern Samar, the Philippines	157 febrile patients who presented to hospitals and 15 afebrile volunteers in the same area	6/157 (3.8%)	4/157 (2.5%)	Not tested	2/157 (1.3%)	–	IFA (<i>R. japonica</i> used for SFGR), single serum sample; 1. Single titer ≥ 1:64

*SFGR = spotted fever group rickettsiae; qPCR = quantitative polymerase chain reaction; IFA = indirect immunofluorescence assay; ELISA = enzyme-linked immunosorbent assay; CI = confidence interval; IIP = indirect immunoperoxidase; JEV = Japanese encephalitis virus; MIA = membrane immunofluorescence assay.

†Convalescent-phase serum sample.

‡None of these patients had positive rickettsial culture or PCR results. Seroconversion for SFGR was noted on for 2 of 13 patients who had paired serum samples.

§*R. rickettsii* (by IFA) and *R. conorii* (by ELISA) were used for detection of SFGR by cross-reactivity. Agreement between different assays (IFA vs. ELISA) was reported.

¶Nine (1%) patients had infections with undetermined rickettsial species.

#Prevalence based on 799 positive diagnostic results.

***R. felis* DNA was detected in 2 patients.

††A total of 12 positive serologic results for 11 patients by IIP.