Annex 14A Etiology of Severe Febrile Illness: Studies of Adolescents and Adults, by Region, 1980–2013

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First Author (Reference)	Location and study dates	Total number of patients in study	Hospital type	Age (population type)	Diagnostic tests conducted	N (%) of diseases searched in review investigated in study	Patients (%) with confirmed infection	Patients infected with HIV (proportion of patients tested)	Most common pathogens
Eastern Africa									
Aarsland and others 2012	Ethiopia, December 2009 - January 2010	102	Urban referral hospital.	1 month –18 years. Primarily children.	DNA extraction and NAAT from malaria blood smears for *S. pneumoniae*, *Salmonella* spp, *Rickettsia* spp, *Borrelia* spp, *Leptospira* spp. (NAAT for *Salmonella* and *S.pneumoniae* did not meet case definitions)	3 (12.0%)	12 (11.8%) with positive NAAT	N.A.	*Plasmodium* spp, *Rickettsia* spp, *Borrelia* spp

Archibald and others 1998	Tanzania; February 1995-April 1995	517	Urban referral hospital	>15 years.	Blood culture. Thick and thin blood smears	2 (8.0%)	145 (28.9%) positive blood culture. 49 (9.8%) malaria slide positive	282 (56.2%)	*Mycobacterium tuberculosis,* Non-typhoidal *Salmonella, S.aureus,*
Bell and others 2001	Malawi; March 1998 - May 1998	238	Urban referral hospital.	>14 years. Primarily adults	Blood culture. Thick and thin blood smears	2 (8.0%)	67 (28.2%) positive blood culture. 72 (31.2%) malaria slide positive	173 (75.9%)	Non-typhoidal *Salmonella, Mycobacterium tuberculosis, Cryptococcus neoformans*
Crump and others 2013	Tanzania; September 2007 - August 2008	870	Urban referral hospital.	Children (>2 years <13 years) Adults >13 years	Blood culture, thick and thin blood smears. Cryptococcal, *S.pneumoniae, H.capsulatum* antigen testing. Leptospirosis and brucellosis standard microscopic agglutination test (MAT). Acute and convalescent serological investigation for Q fever and spotted and typhus group rickettsiosis. NAAT for DENG, CHIKV and flavivirus RNA	11 (44.0%)	Q fever (n=24; 5.0%) spotted fever rickettsiosis (n=36; 8.0%) typhus group rickettsiosis (n=2; 0.4%) chikungunya (n=55; 7.9%) brucellosis (n=16; 3.5%) leptospirosis (n=40; 8.8%)	N.A.	Chikungunya virus, *Leptospira, Rickettsial* spp,

Crump and others 2011	Tanzania; September 2007 - August 2008	403	Urban referral hospital.	>13 years. Primarily adults	Blood culture. Thick and thin blood smears	2 (8.0%)	104 (25.8%) positive blood culture. 8 (2.0%) with malaria slide positive	161(39 %)	*S. enterica* serotype Typhi, *S. pneumoniae, E. coli, Mycobacterium tuberculosis*
Dougle and others 1997	Kenya; July 1994 - October 1994	228	Urban referral, teaching hospital.	> 5 years. Primarily adults	Blood culture. Thick and thin blood smears	2 (8.0%)	51 (22.4%) positive blood culture. 25 (11.0%) malaria slide positive	51 (22.5%)	*S enterica* serotype Typhi, *S.pneumoniae,* Non-typhoidal *Salmonella*
Gordon and others 2001	Malawi; December 1997 - November 1998	9,298	Urban referral teaching hospital.	Unspecified. Primarily adults	Blood culture	1 (4.0%)	449 (16.1%) positive blood culture	N.A.	Non-typhoidal *Salmonella*, *S.pneumoniae, E.coli*
Lofgren and others 2012	Tanzania; August 2007 - September 2008	628	Urban referral medical center and Regional hospital.	>13 years. Primarily adults	*Histoplasma* urine antigen testing	1 (4.0%)	7 (1.1%) positive for histoplasmosis	N.A.	*Histoplasma* spp
McDonald and others 1999	Malawi; August - September 1997	128	Urban referral hospital (Malawi)	> 18 years	Mycobacterial blood culture	1 (4.0%)	14 (10.9%) positive blood culture	101 (78.9%) in Malawi.	Mycobacterium tuberculosis
Meremo and others 2012	Tanzania; June 2011 - December 2011	346	Urban tertiary referral hospital.	Unspecified. Primarily adults	Blood culture	1 (4.0%)	33 (9.5%) positive blood culture	156 (45.0%)	Non-typhoidal *Salmonella*, *S. pneumoniae, E.coli*

Petit and others 1995	Kenya, 1990	336	Study 1 urban and referral	> 8 years. Primarily adults	Blood culture, thick and thin blood smears	2 (8.0%)	Only study 1- 104 (30.9%) positive BSI. 25 (7.4%) malaria slide positive	12 (3.6%)	*Plasmodium* spp, *Salmonella* spp, *E.coli*
Ssali and others 1998	Uganda; January 2007 - April 2007	299	Urban referral, hospital	>15 years.	Blood culture (mycobacterial)	1 (4.0%)	71 (23.7%) positive blood culture	228 (76.3%)	*Mycobacterium tuberculosis, S.pneumoniae*
Western Africa									
Baba and others 2013	Nigeria, July 2008- December 2008	310	Urban, referral, tertiary, teaching hospital	All age groups. Primarily adults	Thick and thin blood smears, Widal test. Plaque reduction neutralization tests for CHIK, YF, DENG, WNV (Did not meet case definitions for Widal and viral tests)	1 (4.0%)	49 (15.8%) malaria slide positive	N.A.	*Plasmodium* spp
Ki-Zerbo and others 2000	Burkina Faso; January 1995 - March 1995	183	Teaching hospital	>15 years	Acute and convalescent serological investigation for spotted and typhus group rickettsiosis and Q fever	2 (8.0%)	17 (5.5%)	N.A.	*Rickettsia* spp (SFG) *Rickettsia* spp (TG) *Coxiella* spp

Afifi and others 2005	Egypt; 1999 - 2003	10,130	Public infectious disease hospital	> 4 years. Primarily adults	Blood culture	1 (4.0%)	1,005 (10.2%) with positive blood culture	N.A.	*Salmonella enterica* serotype Typhi, *Brucella* spp, *S. aureus*
Hyams and others 1986	Sudan; Jan 1984 - Feb 1984	100	Urban hospital	> 12 years. Primarily adults	Blood culture, virology test-isolation and acute and convalescent serological investigation for DENV, YF, WNV, CHIK, thick and thin blood smears	5 (5.0%)	25 (25%) positive blood culture, 21(21%) virus isolation, 13 (13%) malaria slide positive	N.A.	Dengue virus, *Salmonella enterica* serotype Typhi, *Plasmodium* spp
South Central Asia									
Abbasi and others 2009	Pakistan; September 2007 - January 2008	112	Urban teaching hospital	> 13 years. Primarily adults	Thick and thin blood smears. Dengue viral specific immunoglobulin detection (Did not meet dengue case definition)	1 (4.0%)	26 (23.2%) malaria slide positive	N.A.	*Plasmodium* spp

Blacksell and others 2007	Nepal, Kathmandu; July 2002 - June 2004	103	Urban, referral, community general hospital	> 17 years	Blood culture. Serology for scrub typhus, murine typhus, leptospirosis, dengue. Included only for blood culture and paired acute and convalescent sera	3 (12.0%)	29 (28.1%) positive blood culture, 14 (13.5%) confirmed serology	N.A.	*Salmonella enterica* serotype Typhi, *Salmonella enterica* serotype Paratyphi A, *R. typhi*
Chrispal and others 2010	South India; January 2007 - January 2008	398	Tertiary care referral hospital	>16 years	Blood culture, thick and thin blood smears, serological testing for scrub typhus, Dengue virus, *Leptospira* spp, SFG rickettsiosis (did not meet serological case definitions)	1 (4.0%)	32 (8.0%) positive blood cultures, 68 malaria slide positive	N.A.	Salmonella enterica serotype Typhi, *Salmonella enterica* serotype Paratyphi A, *Plasmodium* spp
Faruque and others 2012	Bangladesh; December 2008 - November 2009	462	Six tertiary level, teaching, referral hospital	Unspecified. Primarily adults	Malaria rapid diagnostic test. Serological testing for dengue virus (Did not meet dengue case definition)	1 (4.0%)	3 (0.6%) positive for malaria rapid diagnostic test	N.A.	*Plasmodium* spp

Murdoch and others 2004	Nepal, Kathmandu; Jan 2001 - March 2001 and July - August 2001	876	Urban, general hospital	>14 years old.	Blood culture, Urinary antigen testing, serological testing for IgM antibodies dengue virus, *Leptospira* spp, Scrub typhus and *R. typhi* (did not meet serological case definition)	1 (4.0%)	137 (15.6%) positive blood culture	N.A.	*Salmonella enterica* serotype Typhi, *Salmonella enterica* serotype Paratyphi A
Pattanaik and others 2012	India; 2008 - 2009	67	Teaching hospital	>15 years.	Blood culture, NAAT	1 (4.0%)	No positive results	N.A.	None
Zimmerman and others 2008	Nepal, Kathmandu; Jan 2001 - March 2001 and July - August 2001	756	Urban, tertiary care hospital	>14 years old	*R. typhi* NAAT	1 (4.0%)	50 (6.6%) positive NAAT	N.A.	*R. typhi*
South East Asia									
Archibald and others 1999	Thailand, Bangkok; February 1997 - April 1997	246	Urban, referral, infectious disease hospital.	>15 years.	Blood culture	1 (4.0%)	119 (48.4%) positive blood culture	N.A.	*C. neoformans, Mycobacterium tuberculosis,* Non-typhoidal *Salmonella*

Blair and others 2010	Cambodia; December 2006 - December 2008	4,233	Two referral hospitals	> 2 years	Blood, throat and nasal specimen. rRT- NAAT, virus isolation, HI assay	1 (4.0%)	1151 (27.2%) with confirmed influenza	N.A.	Influenza
Cohen and others 2007	Thailand; February 2002 - February 2003	704	Four district rural hospitals	> 6 years. Primarily adults	Acute and convalescent serological examination for dengue virus, and *Leptospira* spp	2 (8.0%)	199 (28.3%) with confirmed serology	N.A.	Dengue virus, *Leptospira* spp
McDonald and others 1999	Thailand; February 1997 - March 1997 and August - September	216	Urban, referral hospital in Thailand.	> 18 years	Mycobacterial blood culture	1 (4.0%)	20 (9.3%) positive blood culture	154 (71.3%) in Thailand	*Mycobacterium tuberculosis*

Note: N.A. = not applicable. NAAT = nucleic acid amplification test. BSI = bloodstream infection. MAT = microagglutination test. SFG = spotted fever group. TG = typhus group. IgM = immunoglobulin M. rRT = real-time reverse transcriptase. HI = hemagglutination inhibition. spp. = Species.

a. Percentage represents the proportion of patients tested.

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