

Appendix 1 Characteristics of all included studies

Randomized controlled trials and cohort studies

Study ID	Country	Study design	Study duration	Follow-up (weeks)	Person who monitored ADRs	Intervention	Participant		Outcome	
							Primary disease	No. of patient		Age (years) mean, SD
Ceftriaxone vs. Placebo										
Aljfout Q 2016	Jordan	RCT	2014-2015	4	Physician	Ceftriaxone 50mg/kg, bid, 3days	Post-tonsillectomy	90	6.2, 2.3	Nausea and vomiting: 9 Abdominal pain: 7 Fever: 6
						Coamoxiclav 5days		90	6.3, 2.1	Nausea and vomiting: 22 Abdominal pain: 19 Fever: 7
						No intervention		90	6.1, 2.3	Nausea and vomiting: 11 Abdominal pain: 10 Fever: 9
Ceftriaxone vs other generation cephalosporins										
Al-Samman DK 2014	Iraq	RCT	NR	4	Physician	Ceftriaxone 50mg/kg/day, 7days	Impetigo (pyoderma) qd,	26	4.6, 2.1	Pain in injection site: 26 Diarrhea: 0
						Cefadroxil suspension 30mg/kg/day,bid,7days			24	5.2, 1.9

Cannavino CR 2016	America	RCT	NR	4	Physician	Ceftriaxone 75 mg/kg/day (maximum of 4g/days), bid, 72 hours-3days	Community acquired pneumonia	39	3.0, NR	Diarrhea: 2 Vomiting: 4 Pyrexia: 3 Thrombocytosis: 2 Otitis media: 1	
						Ceftaroline 12 mg/kg (if weighing≤33 kg) ;400 mg(if weighing >33 kg), tid; 8 mg/kg (pediatrics aged 6 months or younger),tid			121	4.0, NR	Diarrhea: 8 Vomiting: 2 Pyrexia: 2 Thrombocytosis: 3 Otitis media: 3
Girgis NI 1995	Egypt	RCT	1990-199 3	4	Physician	Ceftriaxone 50-70 mg/kg/day (maximum 4 g/day), qd	Multi-drug resistant Salmonella typhi septicemia	43	10.0, 3.5	No ADR reported	
						Cefixime 15-20 mg/kg/day, q12 h			50	10.3, 2.9	No ADR reported
						Aztreonam 50-70 mg/kg/dose (maximum 8 g/day), q8h			31	9.0, 9.1	No ADR reported
Meng D 2010	China	RCT	2005-200 7	8	Physician	Ceftriaxone 30 – 80 mg/kg/day, qd	Biliary tract infection or	58	Biliary tract infection:	Cholelithiasis: 25	

								pneumonia		3.0, 3.1 Pneumonia: 2.7, 2.4	
							Ceftazidime 50 – 100 mg/kg, qd	50		Biliary tract infection 2.9, 2.5 Pneumonia 2.7, 2.5	Cholelithiasis: 1
Schaad 1990	UB	Berne, Geneva, Lausanne	RCT	1986-1989	1	Physician	Ceftriaxone 100mg/kg/day, qd, 7-9 days	Bacterial meningitis	53	3.1, 3.5	Biliary pseudolithiasis: 16
							Cefuroxime 240 mg/kg/day, q6h , 7-9 days		53	2.6, 2.7	No ADR reported
Ustyol L 2016	Turkey		Prospective cohort	2014-2016	12	Physician	Ceftriaxone 100 mg/kg/day, bid	Infection diseases	86	4.7, 4.9	Biliary lithiasis: 13 Biliary sludge: 5 Nephrolithiasis: 1
							Cefotaxime 150 mg/kg/day, bid		68	4.5, 4.5	Biliary lithiasis: 0 Biliary sludge: 4 Nephrolithiasis: 1
Ceftriaxone vs. Penicillin											
Aljfout Q 2016	Jordan		RCT	2014-2015	4	Physician	Ceftriaxone 50mg/kg, bid, 3days	Post-tonsillectomy	90	6.2, 2.3	Nausea and vomiting:9 Abdominal pain:7 Fever:6
							Coamoxiclav 5days		90	6.3, 2.1	Nausea and vomiting: 22 Abdominal pain: 19

							No intervention		90	6.1, 2.3	Fever: 7 Nausea and vomiting: 11 Abdominal pain: 10 Fever: 9 Diarrhea: 16
Barson 1985	WJ	America	RCT	1982-1983	2	Physician	Ceftriaxone loading dose:75mg/kg, followed by 50 mg/kg ,bid	Bacterial meningitis	27	14.7, NR	Diarrhea: 16
							Ampicillin and chloramphenicol Ampicillin 200 mg/kg/day , Chloramphenicol 100mg/kg/day, qd		23	13.9, NR	Diarrhea: 5
Biner B 2007		Turkey	RCT	2001-2003	4	Physician	Ceftraixone 50 mg/kg, qd	Acute otitis media	34	3.5, 2.4	Diarrhea: 2
							Azithromycin loading dose 10 mg/kg, followed by 5 mg/kg, qd, days 2-5		31	4.5, 2.2	Diarrhea: 2 Vomiting: 1

							Amoxicillin/clavulana te		39	3.6, 2.3	Diarrhea: 3 Vomiting: 1
							90/6.4mg/kg/day, bid,10 days				
Kimata T 2012	Japan	Retrospective cohort	2008-2010	1.6	NR		Ceftriaxone	Bacterial pneumonia	43	2.7, 2.5	Hypercalciuria increase: 5
							91.9±8.0 mg/kg/day, 6.1±1.45 days				
							Amoxicillin		40	2.3, 1.5	No ADR reported
							107±11.8 mg/kg/day, 4.7±1.1 days				
Tuncer 1988	AM Turkey	RCT	1987	24	Physician		Ceftriaxone	Meningococcal disease	20	NR	No ADR reported
							80-100 mg/kg, qd , 4 days				
							Penicillin G		22	NR	No ADR reported
							500,000 units/kg/day, q4h, 5 days				
Ceftriaxone vs. Macrolides											
Arguedas A 2003	Spain	RCT	1995-1997	36	Physician		Ceftriaxone	Uncomplicated acute otitis media	66	2.3, 1.4	Diarrhea: 4 Severe rash: 4 Neutropenia: 8
							50mg/kg, qd				

							Azithromycin 30 mg/kg, qd		66	2.5, 1.3	Diarrhea: 2 Emesis: 3 Rash: 1 Neutropenia: 10
							Azithromycin 10 mg/kg, qd,3days		66	2.7, 1.5	Diarrhea: 3 Neutropenia: 9
Arguedas 2004	A	Costa Rica	RCT	1995-199 7	4	Physician	Ceftriaxone 50 mg/kg,qd	Acute media	otitis 66	2.5, 1.3	Diarrhea: 4 Severe rash: 4
							Azithromycin 30mg/kg,qd,		66	2.7, 1.5	Diarrhea: 2 Emesis: 3 Rash: 1
							Azithromycin 10mg/kg, qd, 3days		66	2.3, 1.4	Diarrhea: 3
Biner B 2007		Turkey	RCT	2001-200 3	4	Physician	Ceftraixone 50 mg/kg, qd	Acute media	otitis 34	3.5, 2.4	Diarrhea: 2
							Azithromycin loading dose10 mg/kg/day, followed by 5 mg/kg, 2-5days		31	4.5, 2.2	Diarrhea: 2 Vomiting: 1
							Amoxicillin/clavulana te 90/6.4mg/kg/day, bid,10 days		39	3.6, 2.3	Diarrhea: 3 Vomiting: 1
Nair 2017		North India	RCT	NR	4	Physician	Ceftriaxone: 75 mg/kg/day, maximum 2.5	Typhoid fever	34	10.4, 3.4	Abadominal pain:5 Vomiting:5 Diarrhoea:12

							<i>g/day, 7 days</i>					Nausea: 7 Anorexia: 6 Skin rash: 0 Abdominal pain: 3 Vomiting: 6 Diarrhoea: 8 Nausea: 5 Anorexia: 3 Skin rash: 1		
							Azithromycin 20 mg/kg/day, maximum 1000 mg/day, 7 days		30		11.4, 3.6			
Ceftriaxone vs. Carbapenems														
Arguedas 2009	A	Costa Rica	RCT	2002-200 3	4	Physician	Ceftriaxone 50 mg/kg/day, bid, 4 days (aged 3 months to 12 years); 50 mg/kg/day (maximum 2 g/d), qd, 4 days (aged 13–17 years)	Complicated urinary tract infection, skin and soft tissue infection, community acquired pneumonia	100		NR		Diarrhea: 10 Vomiting: 2 Infusion site pain: 1 Rash: 1 Infusion site erythema: 2 Decrease in the neutrophil count: 2	
							Ertapenem 30 mg/kg/day, (maximum 1g/d), bid, 4 days (aged 3 months to 12 years) 1g, qd, 4 days (aged 13–17 years)			303		NR		Diarrhea: 18 Vomiting: 6 Infusion site pain: 15 Infusion site erythema: 9 Decrease in the

													neutrophil count: 17
Ceftriaxone vs. Sulfonamides													
Barnett 1997	ED	America	RCT	1991-199 4	4	Physician	Ceftriaxone Maximum 50 mg/kg, qd	Acute media	otitis	241	17.3, 11.6	Diarrhea: 46 Pain at injection site: 19 Rash: 21	
							Trimethoprim-sulfamethoxazole 8mg of TMP and 40 mg of SMZ/kg/day,bid,10day s			243	18, 12.3	Diarrhea: 19 Rash: 14	
Ceftriaxone vs. Monobactams													
Girgis NI 1995	Egypt		RCT	1990-199 3	4	Physician	Ceftriaxone 50-70 mg/kg/day (maximum 4 g) qd	Multi-drug resistant Salmonella		43	10.1, 3.5	No ADR reported	
							Cefixime 15 20 mg/kg/day, q12h	typhi septicemia		50	10.3, 2.9	No ADR reported	
							Aztreonam 50-70 mg/kg/dose (maximum 8 g/day) q 8h			31	9.0, 9.1	No ADR reported	
Ceftriaxone vs. Quinolones													
Leibovitz 2000	E	Israel	RCT	NR	3	Physician	Ceftriaxone 50 mg/kg/day, 3 days, maximum 1 g/day	Acute invasive diarrhea		106	NR	Vomiting: 3 microscopic hematuria: 1	

												impaired liver function: 1
						Ciprofloxacin suspension 10 mg/kg, q12 h, 3 days			95	NR		Vomiting: 5 Arthralgia: 1 Dehydration: 3 Maculopapular rash: 2
Ceftriaxone vs. Chloramphenicol												
Duke T 2003	Australia	Retrospective cohort	1997-2000	12	Physician	Ceftriaxone 50mg/kg,q12h,10-14days	Meningitis		196	0.5, NR		No ADR reported
						Chloramphenicol 25mg/kg,q6h, 10-14days			150	0.6, NR		No ADR reported
Moosa 1989	Durban, South Africa	RCT	NR	3	Physician	Ceftriaxone , 80 mg/kg, qd, 5 days	Bacteriologically confirmed acute typhoid fever	29	8.8, NR			Diarrhea: 1 Abdominal pain: 29 Fever: 29
						Chloramphenicol 12.525 mg/kg, q6h, 3 weeks		30	7.3, NR			Diarrhea: 2 Abdominal pain: 29 Fever: 30

Sawyer 1994	SM	Australia	RCT	1991-199 2	0.7	Physician	Ceftriaxone loading dose 100 mg/kg, qd, followed by 50 mg/kg qd	Epiglottitis	28	NR	No ADR reported
							Chloramphenicol, loading dose 40mg/kg , followed by 25 mg/kg q8h, 5days		27	NR	Urticarial rash :1
High dose Ceftriaxone vs. Low dose Ceftriaxone											
Avci Z 2004		Turkey	Retrospe ctiv cohort	2002-200 3	28	Physician	Ceftriaxone 100mg/kg/day, bid, 57 days	Infectious diseases	24	3.1, 2.5	Renal and urinary disorders Nephrolithiasis:2
							Ceftriaxone 50mg/kg/day, qd, 57days		27	3.1, 2.5	Renal and urinary disorders Nephrolithiasis:2
Kavaliotics 1989		Thessalo niki,Gree ce	RCT	1985-198 7	2	Physician	Ceftriaxone loading dose 100mg/kg,60mg/kg/da y,4,6 and7 days	Bacterial meningitis	26	2.4, 2.3	Mild diarrhea:4
							Ceftriaxone loading dose 100mg/kg,60mg/kg/		26	2.5, 2.2	Mild diarrhea:3

						day, 8,12 and 14 days				
Martin 1990	Swiss	RCT	1983-1985	2	Physician	Ceftriaxone: 100mg/kg/day on day 1 and 2, followed by 60mg/kg/day, 7 days	Bacterial meningitis	47	Range:0.06-15.5	Possibly drug-related fever:6 Skin rash:1 Mild diarrhoea:9 Diaper rash:1 Stomatitis:3
						Ceftriaxone: 100mg/kg/day on day 1 and 2, followed by 60mg/kg/day, 14days		45		Possibly drug-related fever:13 Skin rash:11 Mild diarrhoea:0 Diaper rash:2 Stomatitis:2
						Ceftriaxone: 100mg/kg/day on day 1 and 2, followed by 60mg/kg/day, >10 days		27		Possibly drugrelated fever:7 Skin rash:0 Mild diarrhoea:3 Diaper rash:2 Stomatitis:2
Molyneux2011	Bangladesh, Egypt, Malawi, Pakistan, and	RCT	2001-2006	27	Physician	Ceftriaxone 80–100mg/kg/day ,5days	Purulent meningitis	496	3.2, 3.5	No ADR reported
						Ceftriaxone 80–100		508	3.2, 3.5	No ADR reported

Vietnam						mg/kg/day,10days				
Drug combination										
Molyneux 2017	Blantyre, Malawi	RCT	2010-201 3	24	physician	Benzylpenicillin 50000iu/kg, q8h +Gentamicin 6 mg/kg, 5-14 days	Severe sepsis, pneumonia or meningitis	161	< 7 days: 43 8-30 days : 78 ≥ 30 days :40	Serum bilirubin rise:19
						Ceftriaxone 50-100mg/kg/day, 5-14days		170	<7 days: 34 8-30 days : 93 ≥ 30 days : 43	Serum bilirubin rise:7
						Received both		17	NR	Serum bilirubin rise:1
Uppal 2017	Chandigarh, India	RCT	2012-201 3	12	physician	Ceftriaxone: 50mg/kg, 5 days	Bacterial meningitis	20	3.1, 2.1	NR
						Rifampin+Ceftriaxone: 20mg/kg+50mg/kg,5 days		20	4.1, 3.8	NR

No comparison(cohort study)

Acun C 2004	Turkey	Prospective cohort study	2002-2003	43	Physician	Ceftriaxone: 100mg/kg/day, bid,5-14days	Bacterial infection	35	4.1, 3.6	Gallbladder pseudolithiasis: 3 Gallbladder sludge: 1 Urinary bladder sludge:1
Alemayehu 2014	USA	Retrospective cohort study	NR	219	Physician	Ceftriaxone: 50mg /kg/day, qd, 8.7 4 days	Perforated appendicitis	71	10.8, 3.8	Stones or sludge in the gallbladder: 10
Baran 2017	Adana; Turkey	Retrospective cohort	2009-2006	NR	physician	Ceftriaxone	Cholelithiasis	74	7.5, 4.3	Cholelithiasis:3
Bradley JS1992	Canada	retrospective cohort study	1985-1988	154	Physician	Ceftriaxone: 20-50mg/kg/day, qd , 13.4 days	Infections	41	NR	Diarrhea: 1 Slight induration at one injection site: 1
Chaudhary 2017	India	Prospective cohort	2011-2015	NR	physician	ceftriaxone+ sulbactam+ disodium edetate: 30-75mg/kg/day (maximum120mg/kg)	Extended spectrum beta lactamases/metallo beta lactamases infections	750	11.9, 3.2	Vomiting 10 Pain at injection site 12 Nausea 4 Thrombophlebitis 5 Localized pain 2 Fever 4 Itching 2 Mild rashes 1
Chaudhary 2018	India	Prospective	2011-2012	NR	Physician	Ceftriaxone+sulbactam+disodiumedetate:	Hospital-acquired pneumonia	450	9.4, 5.9	Pain at injection:16 Fever:12

		cohort				<12 years old: 75mg/kg/day; years old:1.53g/day	>12				Vomiting:10 Nausea:8 Thrombophelibitis:5 Itching:2 Localised pain:2
Ceran C2004	Turkey	Prospective cohort study	NR	NR	Physician	Ceftriaxone: 100mg/kg/day,3-10 days	Intra-abdominal infections and surgical prophylaxis	50	8.0, NR		Biliary sludge: 1 pseudolithiasis: 12
Congeni BL1986	America	Prospective cohort study	1984-1985	64	Physician	Ceftriaxone: loading dose 100 mg/kg/day, followed by 80mg/kg , 5-28days	Bacterial meningitis	57	2.3, NR		Stasis in injection site erythematous rash: 1 Trush: 1 Diarrhea:11 Diaper dermatitis:1
Del RM1982	America	Prospective cohort study	1981	NR	Physician	Ceftriaxone: loading dose 75mg/kg/day, followed by 50mg/kg/d, q8h, 45 days	Bacterial meningitis	32	1.0, NR		No ADR reported
Mohkam M2007	Iran	Prospective cohort study	2003-2005	12	Physician	Ceftriaxone 75mg/kg/day, 9-10 days	Pyelonephritis	284	2.7, 2.1		Kidney stone:4
Murata S2015	Japan	Prospective	2010-2011	20	Physician	Ceftriaxone:	Acute disease	60	NR		Biliary pseudolithiasis:

		ive cohort study	1				60-100mg/kg/day, 3-10 days				11
Nelson SJ1985	USA	Prospective cohort study	NR	3	Physician	Ceftriaxone: 68-100mg/kg/day, 3-20 days	Serious infections	12	5.5		Abnormal pain:1 Local irritation/skin rash:1
James J1985	England	Prospective cohort study	NR	32	Physician	Ceftriaxone: 50mg/kg/day, qd, 8months	Suspected or proven sepsis	104	0.6, 0.002		No ADR reported
Grubbauer HM1990	Austria	Prospective cohort study	1985-1989	219	Physician	Ceftriaxone: 100 mg/kg/day, qd,13 days (median)	Bacterial meningitis	33	Range:0.4-15		Neutropenia:1 transient elevation of glutamic oxaloacetic transaminase: 1 Cholelithiasis:1 Persistent hearing deficiencies:2
Higham M1985	America	Prospective cohort study	NR	NR	Physician	Ceftriaxone: 50mg/kg/day, qd, 3-22days	Bacterial infections	34	Range:0.2-14		Diarrhea: 7 Rash : 5 Neutropenia: 1 Eosinophilia:2
Bor B 2004	Turkey	Prospective cohort	NR	13	Physician	Ceftriaxone: 100 mg/kg/day, 7days	Bacterial meningitis	38	5.2, 0.7		Cholelithiasis :13 Biliary sludge: 3

			study								
Palanduz A2000	Turkey	Prospective cohort study	1995-1997	5	Physician	Ceftriaxone: 100mg/kg/day, 1-3weeks	Severe infection	118	Abnormal: 5.3, 3.5 Normal:3.9, 2.8	Gallbladder sludge:8 Biliary pseudolithiasis:12	
Soysal A2007	Turkey	Prospective cohort study	2001-2003	2	Physician	Ceftriaxone: 3-14days	Bacteria infections	114	3.8, 3.9	Biliary sludge: 20 Cholelithiasis : 15	
Tuna KC2016	Turkey	Retrospective cohort study	2008-2013	NR	Physician	Ceftriaxone	Cholelithiasis	254	8.9, 5.2	Cholelithiasis: 51	
Zhuang WL2005	China	Prospective cohort study	2004-2005	8	Physician	Ceftriaxone: 70-100mg/kg/day, 1week	Pneumonia, cholecystitis	47	Range:1.8 - 12	Emesis: 22 Stomachache: 16	
Yogev R1986	America	Prospective cohort study	NR	NR	Physician	Ceftriaxone: Non-central nervous system infections:50 mg/kg Central nervous system infections: loading dose 100 mg/kg/day, followed by 80 mg/kg/day, qd	Serious infections	71	0.04-15	Diarrhea: 7 Fever: 1 High fever:1 Arthralgia: 1 Rash: 1 Urticarialike rash:1	

Danker WM1988	USA	Prospective cohort study	1984-198 5	73	Physician	Ceftriaxone: loading dose 100mg/kg/day followed by 80 mg/kg/day	Bacterial meningitis	22	1.5, NR	Diarrhea: 7 Fever: 3 Haematological thrombocytosis: 17 Neutropenia: 2
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Note: ADR: Adverse drug reaction; CNS: central nervous system; IQR: interquartile range; NR: Not Reported.

Case-control studies

Study ID	Country	Study duration	Case and control	No. of patient	Age (years) mean, SD	No. of patient use ceftriaxone (%)
Ferrajolo C 2016	Italy; Netherlands	2002-2008	Case: Children with liver injury	938	11.3, 5.1	3 (0.3%)
			Control: Children without liver injury	93, 665	11.4, 5.2	37 (0.0%)

Case series

Study ID	Country	Source of case and control	No. of patient	Primary disease	Age(years) (mean, SD)	Male (%)	Ceftriaxone exposure	ADR
Araz N2007	Turkey	Hospital	8	Meningitis	6, 2	87.5%	100 mg/kg, 7 ± 1 days	Pseudolithiasis
Shen X2014	China	Hospital	15	NR	4.8, 3.7	80.0%	1g/day, 5 days	Urolithiasis (acute kidney injury)

Note: NR: Not Reported

Case reports

Study ID	Country	Source of case	Primary disease	Age(y ears)	Sex	Drug exposure	ADRs
AlHawsawi ZM2010	Saudi Arabia	Hospital	Sickle cell anemia	5	Male	Ceftriaxone	Haemolysis Anaphylactic reaction Skin rash Fever Chills Hypotensive

Bernini JC1995	America	Medical Center	Sickle cell anemia	2	Male	Ceftriaxone 75mg/kg, 14 doses	Schock Bilateral pneumonic infiltrate Multiorgan failure syndrome Immune hemolytic anemia Hemoglobinuria Unresponsive Cardiorespiratory arrest Multiple organ failure(MOF) Death
Bell MJ2005	America	Medical center	Sickle cell anemia	17	Female	Ceftriaxone Azithromycin	Haemolytic anaemia Red urine Hepatitis Debris in the gallbladder Cardiac arrest Death
Boggs SR2011	America	American academy of pediatrics	Lyme arthritis	11	Female	Ceftriaxone	Hemolysis Fever with shaking chills Worsening knee pain immediately Emesis Abdominal pain Anorexia with mild diarrhea Rapidly decreasing hemoglobin level Renal failure
BorgnaPignatti C1995	Italy	Hospital	HIV	8	Male	Ceftriaxone 80mg/kg/d	Immune haemolytic anaemia Chest tightness Back pain

Candemir M2006	Turkey	Hospital	Pyelonephritis	0.7	Male	Ceftriaoxne 500mg/d Cefotaxime 150 mg/kg/d, 3 days Cefixime 4 mg/kg/d	Dyspnea Bilateral pulmonary infiltrates Hemoglobinuria Death Autoimmune hemolytic anemia Hepatomegaly
Citak A2002	America	University	No underlying immune deficiency or haematologic disease	5	Female	Ceftriaxone 50mg/kg/d	Immune haemolytic anaemia Seizures recurred
Corso M2005	America	University	Sickle cell anemia	10	Male	Ceftriaxone	Immune haemolytic anaemia Myocardial Ischemia Unresponsive Extremely pale
Demirkaya E 2006	Turkey	Medical Academy	No underlying immune deficiency or hematologic disease	5	Female	Ceftriaxone	Immune hemolytic anemia(IHA) Paleness Oliguria Acute renal failure (ARF)
Döneray H	Turkey	Hospital	Purulent	6	Female	Ceftriaxone	Immune haemolytic anaemia

2009			meningitis		le	100mg/kg/day		Pale Vomiting Tachypnea Back pain Acute renal failure
Doratotaj S 2009	America	Hospital	Resected astrocytoma	infant 4	Fema le	Ceftriaxone 50mg/kg/d		Hemolysis Apneic and bradycardic Disseminated intravascular coagulopathy Acute renal failure
Goyal M 2011	America	Hospital	Hemoglobin sickle cell	2	Male	Ceftriaxone 2 days		Immune haemolytic anaemia Blood pressure fell to 69/30 mm Hg Pale Capillary refill time increased
				10	Fema le	Ceftriaxone 2weeks		Immune haemolytic anaemia Acute mental status changes Incontinent of bowel and bladder Acute renal failure Death
Großjohann B 2004	Germany	Hospital	Wrists and swelling	redness 9	Male	Ceftriaxone 2g/d, 13 days		Thrombocytopenia
			Pneumococcal meningitis	16	Fema le	Ceftriaxone 4g/d,9 days		Immune haemolytic anaemia Acute dizziness Tachypnoe Extreme paleness Acute renal failure Death

Kakaiya R 2004	America	Medical center	Sickle cell anemia	10	Male	Ceftriaxone 3 days	Acute hemolysis Generalized seizures Loss of consciousness Respiratory failure Cardiac arrest
Kapur G 2006	America	Hospital	Craniosynostosis	10	Male	Ceftriaxone 1g/, bid Clindamycin 250 mg, q6h	Immune haemolytic anaemia Acute Renal Failure maculopapular rash
Lascari AD 1995	America	Hospital ,Medical College	Juvenile chronic myelocytic leukemia	5	Male	Ceftriaxone 50 mg/kg/d + amoxicillin	Immune hemolytic anemia Ear pain Cardiac arrest Death
Liu W 2014	China	Hospital	Acute laryngotracheal bronchitis.	4	Female	Ceftriaxone 1.5 g/d	Immune hemolytic anemia weakness, minor abdominal discomfort manifested transient urticaria
Mattis LE 2004	America	Hospital	Crohn's disease	9	Male	Ceftriaxone 75mg/kg/d, 7 days	Immune haemolytic anaemia Back pain Vomiting Tachycardic Tonic/clonic seizure Acute renal failure Liver function worsen

Meyer O1999	NR	Hospital	Pneumococcal meningitis	16	Female	Ceftriaxone 7 days	Immune haemolytic anaemia Muscle spasms Dizziness Tachypnea Pulmonary embolism Acute renal failure Death
Moallem HJ 1998	America	Hospital	HIV	14	Female	Ceftriaxone 60mg/kg/d	Immune haemolytic anaemia Severe back pain Nauseated, vomited, and collapsed. Death
Northrop MS 2015	America	Hospital	Crohn disease	14	Male	Ceftriaxone	Hemolytic Anemia abdominal pain nonbloody vomiting back pain, headache
Pecker LH 2016	America	Hospital	lowgrade glioma	5	Male	Ceftriaxone 50 mg/kg/d	Immune hemolytic anemia abdominal pain vomiting hypotension
Quillen K 2008	America	Hospital	HIV	11	Male	Ceftriaxone	Hemolysis Hemoglobinuria Hypotension Disseminated intravascular coagulation Acute renal failure Death
Reis boto ML	Portugal	Hospital	Hemoglobin	1.7	Male	Ceftriaxone	Severe immune haemolytic anaemia

2011			sickle cell					Shock
Schuettpelz LG 2009	America	Hospital	Sickle cell disease	6	Female	Ceftriaxone 50 mg/kg/d		Immune haemolytic anaemia Incontinent, and unresponsive urine become dark brown
Scimeca PG1996	America	Hospital	Hypereosinophilic syndrome	3	Female	Ceftriaxone 75 mg/kg/d		Severe hemolysis Hypotension Unresponsive Cardiovascular collapse Oliguria Death
Tobian AA 2010	America	Hospital	hemophagocytic lymphohistocytosis	7	Male	Ceftriaxone		Immune haemolytic anaemia Abdominal pain, vomiting Hematuria Back pain Hypotension
Vanburen 2018	American	Hospital	Congenital nephrotic syndrome	9	Female	Ceftriaxone 2g/d		Immune hemolysis Unresponsive Decrease in pulse oxygenation Hypotensive Extremely pale Multiorgan system failure Disseminated intravascular coagulopathy Cerebral edema Uncal herniation Increased intracranial pressure Brain dead

Yuri V 2000	Israel	Hospital	Sickle cell anemia	6	Male	Ceftriaxone 75 mg/kg/d	Immune haemolytic anaemia Suddenly abdomen pain Chronic hepatosplenomegaly
Kudva Patel V 2002	America	Hospital	Hand infection	5	Male	Ceftriaxone 2 g/d	Xlinked agammaglobulinemia maculopapular rash
Blais C 1994	Canada	Department of Radiology	Extensive cellulitis	1.5	Male	Ceftriaxone loading dose 80 mg/kg, followed by 50mg/kg/d, q12h	Biliary pseudolithiasis Enlarged painful gallbladder
R.A.de M 1999	Netherlands	Hospital	Acute bacterial meningitis	7	Male	Ceftriaxone 125 mg/kg/d	Biliary pseudolithiasis Nephrolithiasis Transient impairment of renal function Biliary sludge
Acun C 2004	Turkey	University	Acute bacterial meningitis	5	Female	Ceftriaxone 100 mg/kg/d	Biliary Pseudolithiasis Urinary bladder sludge Abdominal pain Abdominal distension
Wang YQ 2004	China	Hospital	Fever and throat pain	7	Female	Ceftriaxone 2g/d	Biliary pseudolithiasis
Zhang XM 2004	China	Hospital	Typhoid fever	6	Male	Ceftriaxone 100mg/kg/d+ ampicillin 150mg/kg/d	Biliary pseudolithiasis
Kutuya N 2008	Japan	Hospital	Pneumonia	5	Male	Ceftriaxone 2 g/d, bid	Biliary pseudolithiasis
John Solomon	India	Hospital	Meningitis	8	Male	ceftriaxone 100mg/kg/d	Pseudolithiasis

P 2015								abdominal pain
Zhong XH 2010	China	Hospital	Nephrotic syndrome	11	Male	Ceftriaxone 2g/d,3 days		Biliary pseudolithiasis
			Acute poststreptococcal glomerulonephritis	10	Male	Ceftriaxone 1.5g/d,6 days		Biliary pseudolithiasis
			Nephrotic syndrome	12	Male	Ceftriaxone 2g/d,2weeks + Metronidazole 2weeks		Biliary pseudolithiasis
Von Martels JZH 2013	Netherlands	Hospital	Lyme arthritis	14	Male	Ceftriaxone 4g/d,2weeks		Biliary Pseudolithiasis Abdominal pain
Du 2018	China	Hospital	Headache and fever urinary and fecal incontinence	9	Male	Ceftriaxone 2g,bid,i.v., 50days		Biliary pseudolithiasis Gallbladder sediment Liver function worsen
Jacobs 1988	RF America	Hospital	Septic arthritis and osteochondritis	16	Female	Ceftriaxone 2g/d, bid, i.v.		Cholelithiasis Nausea Vomiting Anorexia Abdominal pain
Lemberg D 2005	Australia	Hospital	Meningitis	6.7	Female	Ceftriaxone Acyclovir		Cholelithiasis Abdominal pain Nausea

									Fever
Robertson FM 1996	America	Hospital	Open head trauma	9	Male	Ceftriaxone 100mg/kg/d,bid			Cholelithiasis Epigastric abdominal pain, crampy
Ravisha MS 2004	India	Hospital	Direct hyperbilirubinemia	17	Male	Ceftriaxone 50 mg/kg/d, bid, i.v +Amikacin7.5mg/kg/d, bid, 7days			Cholestasis Progressive icterus High colored urine
Peker E 2009	Turkey	Hospital	Tonsillitis	12	Male	Ceftriaxone 50 mg/kg/d			Toxic hepatitis Weakness and fatigue
Kang MH 2014	America	Hospital	Relapsed/refractory stage 4 high risk neuroblastoma	7	Male	Ceftriaxone +acetaminophen			Hepatic toxicities(liver injury) Grade 1 abdominal pain (had not stooled in five days) Grade 2 headache
Stojanovic V 2009	Serbia	Hospital	HenochSchonleinpurpura	12	Female	Ceftriaxone 100 mg/kg/d			Fever Nephrolithiasis Intensive pain in the abdomen Vomited several times
Milosvic D 2013	Croatia	Hospital	Streptococcus intermedius subdural empyema	11	Male	Ceftriaxone 100mg/kg/d,13 days			Nephrolithiasis
Lozanovski VJ 2011	Fyrom	Hospital	Community acquired pneumonia	5	Male	Ceftriaxone 1.0g/d			Urolithiasis Moderate hypercalciuria Intensive right sided lumbar pain
Akl KF 2011	Jordan	Hospital	Meningitis	2	Male	Ceftriaxone 100mg/kg/d			Acute urinary retention (AUR) Associated with suprapubic pain and tenderness
Kimata T 2012	Japan	Hospital	Acute bacterial	1	Male	Ceftriaxone			Urinary sludge

				meningitis			120 mg/kg/d Meropenem 120 mg/kg/d	White turbid urine
Ernst MR2002	Netherlands	Hospital		High fever and a petechial rash	3	Male	Ceftriaxone 100mg/kg/d	Anaphylaxis Excitation with overstretching Generalized papular urticarial rash developed Tachycardia Capillary refill time increased
Arslankoylu AE 2011	Turkey	University Medical Faculty		Pharyngitis.	2	Male	Ceftriaxone 1.5mg/kg	Anaphylaxis Cyanosis Hypotension Flushing Respiratory arrest Circulatory failure
Shrestha D 2013	Nepal	Medical college Teaching Hospital		Nonbilious projectile vomitings	9	Male	Ceftriaxone 50mg/kg/d	Anaphylaxis Generalized maculopapular pruritic rashes Heart rate increased Peripheral pulses become feeble. Capillary refill time increased Hypotension Unresponsive Fever SpO2 decrease
Agrawal SR 2014	India	Institute of Medical Sciences		Palpable purpura	17	Female	Ceftriaxone 1g, q12h	Leukocytoclastic vasculitis Acute allergic interstitial nephritis Facial puffiness

Kline A 2016	Australia	Hospital	Pustular rash	11	Female	Ceftriaxone Flucloxacillin	Anasarca Decrease urine output Reddish palpable purpuric nonblanching rash Acute generalised exanthematous pustulosis; Rash Febrile Neutrophilia
Ravi J 2001	America	Hospital	Aseptic meningitis	16	Female	Ceftriaxone 2g/d	Erythema Migrans
Arulraj R 2013	India	Medical College and Research Institute	Fever, cough and cold	7	Male	Ceftriaxone	Mimicking measles urticarial lesions maculopapular lesions Rash Audible wheeze Loose stools Vomiting
Chedrawi AK 2004	Saudi Arabia	Hospital	Chronic renal insufficiency secondary to congenital renal dysplasia	12	Female	Ceftriaxone 50 mg/kg, q12h	Nonconvulsive Status Epilepticus Spontaneous eye opening Occasional mumbling Visual hallucinations
Sharma N 2012	India	Medical College	Diarrhea and high grade fever	8	Male	Ceftriaxone 1g/d	Acute reversible encephalopathy Progressive apathy Somnolence
Yalmaz S 2011	Turkey	Hospital	Urinary	0.4	Male	Ceftriaxone	Vitamin K deficiency

tract infection

ADR = Adverse drug reaction; RCT = Randomized controlled trial; NR = Not reported.

List of included studies**Randomized controlled trials**

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