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Clinical characteristics, treatment and outcomes of paediatric COVID-19: a systematic review and meta-analysis

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ABSTRACT

Objective Compare paediatric COVID-19 disease characteristics, management and outcomes according to World Bank country income level and disease severity.

Design Systematic review and meta-analysis.

Setting Between 1 December 2019 and 8 January 2021, 3350 articles were identified. Two reviewers conducted study screening, data abstraction and quality assessment independently and in duplicate. Observational studies describing laboratory-confirmed paediatric (0–19 years old) COVID-19 were considered for inclusion.

Main outcomes and measures The pooled proportions of clinical findings, treatment and outcomes were compared according to World Bank country income level and reported disease severity.

Results 129 studies were included from 31 countries comprising 10251 children of which 57.4% were hospitalised. Mean age was 7.0 years (SD 3.6), and 27.1% had a comorbidity. Fever (63.3%) and cough (33.7%) were common. Of 3670 cases, 44.1% had radiographic abnormalities. The majority of cases recovered (88.9%); however, 96 hospitalised children died. Compared with high-income countries, in low-income and middle-income countries, a lower proportion of cases were admitted to intensive care units (ICUs) (9.9% vs 26.0%) yet pooled proportion of deaths among hospitalised children was higher (relative risk 2.14, 95% CI 1.43 to 3.20). Children with severe disease received antimicrobials, inotropes and anti-inflammatory agents more frequently than those with non-severe disease. Subgroup analyses showed that a higher proportion of children with multisystem inflammatory syndrome (MIS-C) were admitted to ICU (47.1% vs 22.9%) and a higher proportion of hospitalised children with MIS-C died (4.8% vs 3.6%) compared with the overall sample.

Conclusion Paediatric COVID-19 has a favourable prognosis. Further severe disease characterisation in children is needed globally.

INTRODUCTION

The coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 has spread from a local outbreak in China to a global pandemic within months. On 31 December 2019, a cluster of cases with pneumonia of unknown cause emerged from Wuhan, China. On 30 January 2020, the WHO declared the coronavirus outbreak a Public Health Emergency of

International Concern, and on 11 March 2020, a pandemic. As of 21 January 2021, there have been over 95.6 million confirmed COVID-19 cases and over 2.0 million associated deaths from 216 countries, areas or territories.¹ Children under-19 years of age comprise a small proportion (1%–10%) of the total reported cases^{2–5} with a lower risk of developing critical illness from COVID-19 infection compared with adults.⁶ Prior systematic reviews of paediatric COVID-19 have described a mild disease in children with good outcomes.^{4 7 8} Since the publication of these reviews, the pandemic has spread extensively around the globe. In addition to pulmonary manifestations of COVID-19 in children, reports from Europe, North America, Latin America and Asia have emerged, describing a multi-system inflammatory syndrome children (MIS-C) related to COVID-19 infection.^{9–12} COVID-19 has also disrupted essential maternal and child health interventions, including outpatient visits and vaccinations for young children in most countries, further worsening the existing burden on health-care provision and delivery.¹³

The objective of this review, in addition to providing a comprehensive update of the evolving paediatric COVID-19 literature, is a unique comparison of reported cases in low-income and middle-income countries (LMICs) to high-income countries (HICs) and of children with severe versus non-severe disease. Furthermore, the review provides a subgroup analysis of children presenting with symptoms of MIS-C and neonatal cases.

METHODS

The protocol of the review is registered with PROSPERO (CRD42020183134). This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA).

SEARCH METHODS

The review includes a comprehensive search of MEDLINE, Embase, WHO COVID-19 Database, Chinese COVID-19 Databases (CNKI and Wangfang), Latin-American and Caribbean Health Sciences Literature (LILACS) from 1 December 2019 to 8 January 2021. Complementary searches were conducted in Google Scholar, John Hopkins Health Resource, WHO news and the Chinese and US CDC Library. MedRxiv, BioRxiv and ChinaXiv

were searched for preprints. No language restrictions were applied.

A search strategy was formulated and administered as shown in online supplemental table 1.

STUDY SELECTION

Observational studies reporting children (0–19 years old) with laboratory-confirmed COVID-19 (serology or RT-PCR) were considered for inclusion. Studies with a subset of children 0–19 years were included if disaggregated data for children were provided. Studies were screened for any overlap in paediatric cases by reviewing institution details and the period reported. Review articles, case reports, commentaries and letters not presenting any original data were excluded. Case reports were excluded to reduce risk of selection bias and over-representation of extreme cases. Covidence Software (2016) was used for screening by two reviewers independently and in duplicate. Key reference lists were screened for additional studies.

DATA EXTRACTION

Two reviewers conducted data extraction using a prepiloted data form. Data extracted included authors' names, date of publication, study-design, city, country, number of cases, gender, comorbidities, travel and contact history, diagnostic tests for COVID-19, clinical details, laboratory tests, radiological findings, management and outcomes. Disaggregated data by age groups (0–5 years, 5–10 years and >10 years old) and reported disease severity was extracted where available. Criteria for severe disease were as defined within each individual study and included admission to intensive care units (ICUs), use of mechanical ventilation, multiorgan failure and presence of hypoxia (oxygen saturation <92%).

QUALITY ASSESSMENT

Individual study quality was evaluated independently by the review authors using quality assessment tools developed by the National Heart Lung and Brain Institute (NHLBI)¹⁴ (<https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>). Study quality was scored out of 8, based on clarity of study objectives, case definition, consecutive inclusion of cases, comparability of included patients, definition and measurement of outcomes, length of follow-up, statistical methods and results. Studies with score 6–8 were considered to be good quality, 4–5 considered fair quality and <4 considered poor quality.

DATA SYNTHESIS

Categorical data were summarised as counts and proportions. The pooled proportions of reported findings were calculated using Comprehensive Meta-Analysis 2.2.027 using random-effects model. I^2 was calculated to examine statistical heterogeneity ($I^2 > 50\%$ considered high heterogeneity). The clinical features and outcomes were compared according to (1) World Bank country income level (HICs versus LMICs)¹⁵ and (2) reported disease severity (severe versus non-severe) using pooled proportions and their 95% CIs, supplemented by relative-risk (RR). Subgroup analyses of children with MIS-C and neonatal cases were conducted.

RESULTS

After removal of duplicates, 3350 citations were screened for inclusion. Full texts of 198 studies were screened and 129 studies^{2 3 9–12 16–138} were included (online supplemental figure 1). Sixty-nine studies were excluded as they either presented

overlapping data, did not provide age-disaggregated data for children or were commentaries, editorials or reviews. In terms of study setting, 13 studies were population-based national surveillance studies, 94 studies included only children admitted to hospital and 22 studies reported patients presenting to outpatient clinics or emergency departments (hospitalisation rate of 24.2%, 385/1590).

Sixty studies were from HICs (n=6528) and 69 studies from LMICs (n=3723). Almost one-third of included studies were from China (36/129, 28.0%),^{216–3335 37–43 45 52 53 55–57 71 74 138} one-fifth were from the USA (24/129, 18.6%)^{3 9 10 47 58 60 64 68–70 79 81 82 85–87 93 98 109 110 115 120 133 136} together comprising almost half of the included sample size (n=4758, 46.4%). The country of origin of included studies and study characteristics are summarised in online supplemental figure 2, tables 2 and 3.

DEMOGRAPHICS AND EPIDEMIOLOGY

A total of 9335 children from the 129 case series were included in the meta-analysis. Of 8455 children for whom initial disposition was reported, 4851 were hospitalised (57.4%). Among them, 55.5% were men. The patient's ages ranged from 0 to 17 years with mean age of 7.0 ± 3.6 years. Ninety-one of the 129 studies reported age-disaggregated data for infection incidence as shown in online supplemental table 4. Nearly half of the cases were >10 years of age. Contact exposure to COVID-19 was reported in 64.0% of cases. Travel history to an epicentre was reported in 13.0% cases. At-least one underlying comorbidity was reported in 27.1% of cases. The most common reported comorbidities were immunosuppression (15.8%) and lung disease (12.5%).

CLINICAL MANIFESTATIONS

Table 1 summarises the clinical manifestations reported in the studies. There were 13.1% asymptomatic cases (95% CI 10.4% to 16.3%) who presented primarily through contact exposure in family-clusters (parents, siblings and other relatives). The most common presenting symptoms were fever (63.3%, 95% CI 58.6% to 68.4%) and cough (33.7%, 95% CI 29.6% to 38.1%) followed by nausea or vomiting (20.0%, 95% CI 16.5% to 24.0%) and diarrhoea (19.6%, 95% CI 16.1% to 23.7%). Other symptoms included dyspnoea, nasal-symptoms, rashes, kawasaki-like symptoms, conjunctivitis, fatigue, abdominal pain and neurological symptoms. Sixty-seven of the 129 studies reported age disaggregated data for clinical features (online supplemental table 5). Clinical features were similar in the three age groups: ≤ 5 years, >5 to ≤ 10 years, >10 years with higher prevalence of abdominal symptoms in children >5 years.

RADIOLOGICAL AND LABORATORY FINDINGS

One thousand five hundred and thirty cases out of 3670 (44.1%, 95% CI 39.5% to 48.9%) cases had radiological abnormalities; ground glass opacities (27.4%) were the most commonly reported abnormality.

Sixty-six studies provided details on laboratory-markers (table 2). Pooled analysis revealed increased C-Reactive Protein (CRP) (54.2%, 95% CI 41.5% to 66.3%), serum-ferritin (46.7%, 95% CI 32.3% to 61.7%), lactate dehydrogenase (LDH) (36.5%, 95% CI 26.5% to 47.8%) and d-dimers (35.2%, 95% CI 22.1% to 51.0%) as the most common abnormalities. Other reported abnormalities included elevated erythrocyte sedimentation rate (ESR), lymphopaenia, procalcitonin and biomarkers for organ

Table 1 Clinical symptoms among reported paediatric COVID-19 cases

Characteristics	Events/total patients	Mean proportion % (95% CI)	Heterogeneity I ² (%)
Comorbidity	1590/6086	27.1 (23.1 to 31.5)	37.6
Fever	3576/6296	63.3 (58.6 to 68.4)	34.9
Cough	1807/5261	33.7 (29.6 to 38.1)	34.4
Nausea/vomiting	880/4243	20.0 (16.5 to 24.0)	25.7
Diarrhoea	796/4884	19.6 (16.1 to 23.7)	13.4
Dyspnoea	879/5332	17.5 (14.4 to 21.1)	23.7
Nasal symptoms	1080/5406	16.6 (13.9 to 19.7)	10.6
Rashes	744/4387	15.5 (11.9 to 19.9)	25.9
Fatigue	709/4474	15.5 (12.6 to 19.3)	26.3
Abdominal pain	626/4135	15.3 (11.9 to 19.4)	26.5
Kawasaki shock/sign	821/4365	13.3 (9.8 to 17.9)	30.6
Asymptomatic	1114/6084	13.1 (10.4 to 16.3)	15.4
Neurological symptoms	693/5475	12.1 (10.1 to 14.6)	17.6
Conjunctivitis	529/4998	10.5 (7.8 to 14.0)	21.0
Pharyngeal erythema	428/3638	9.0 (6.7 to 12.0)	0.0

injury including elevated levels of pro B-type natriuretic peptide, troponin and creatine kinase-MB as shown in [table 2](#).

MANAGEMENT

Details of clinical management are as shown in [table 3](#). Commonly used therapies among hospitalised children were antimicrobials (32.2%, 95% CI 25.2% to 40.1%), intravenous immunoglobulin (IVIG) (19.5%, 95% CI 13.5% to 27.2%) and systemic-steroids (19.3, 95% CI 14.9% to 24.9%). Other treatment regimens included aspirin, inotropic drugs, inhaled interferon- α (IFN- α), antimalarials and antivirals (ribavirin, oseltamivir, lopinavir,

ritonavir and litonavir). Mechanical ventilation was provided to 490 patients (12.2%, 95% CI 9.7% to 15.3%).

PROGNOSIS AND SEVERE CASES

One thousand three hundred and fifty-nine patients (22.9%, 95% CI 17.6% to 29.2%) were admitted to ICUs ([table 3](#)). Thirty-eight studies provided disaggregated data for severe cases ([table 4](#)). A higher proportion of children with severe disease had symptoms consistent with MIS-C and received antimicrobials, inotropes and anti-inflammatory agents compared with those with non-severe disease. There were no deaths among children

Table 2 Laboratory and radiological features among reported paediatric COVID-19 cases

Characteristics	Events/total patients	Mean proportion % (95% CI)	Heterogeneity I ² (%)
Inflammatory marker			
CRP \uparrow	556/1165	54.2 (41.5 to 66.3)	21.4
Ferritin \uparrow	247/525	46.7 (32.3 to 61.7)	46.5
LDH \uparrow	356/922	36.5 (26.5 to 47.8)	35.6
Procalcitonin \uparrow	137/879	21.3 (12.2 to 34.5)	24.9
Leukocytes \uparrow	138/953	19.9 (13.3 to 28.8)	21.4
Lymphocytes \downarrow	359/1347	19.0 (12.8 to 27.1)	0.0
ESR \uparrow	248/838	18.9 (11.8 to 28.9)	0.0
IL-6 \uparrow	41/341	13.1 (5.5 to 28.2)	7.1
Leucopaenia (+)	77/1037	10.7 (7.7 to 14.6)	0.0
Lymphocytes \uparrow	66/1264	8.2 (4.9 to 13.5)	0.0
Neutrophils \uparrow	22/574	7.8 (4.8 to 12.4)	0.0
Biomarkers for organ injury			
proBNP \uparrow	211/441	45.5 (28.5 to 63.5)	49.5
Troponin \uparrow	239/703	39.7 (24.7 to 57.0)	30.5
LFTs \uparrow	287/816	29.8 (20.3 to 41.6)	10.8
CKMB \uparrow	82/293	25.5 (13.4 to 43.0)	31.1
RFTs \uparrow	86/344	17.6 (7.6 to 35.6)	23.6
Coagulopathy markers			
D-dimers \uparrow	272/711	35.2 (22.1 to 51.0)	19.1
Fibrinogen \uparrow	168/438	17.5 (7.6 to 35.4)	0.0
Radiological test			
Abnormal CXR/CT	1530/3670	44.1 (39.5 to 48.9)	35.0

Table 3 Clinical management and outcomes among reported paediatric COVID-19 cases

Characteristics	Events/total patients	Mean proportion % (95% CI)	Heterogeneity I ² (%)
Clinical management			
Antibiotics	1345/3610	32.2 (25.2 to 40.1)	41.9
IVIg	698/3522	19.5 (13.5 to 27.2)	18.4
Systemic steroids	801/4229	19.3 (14.9 to 24.9)	23.7
Antiviral	527/4019	15.3 (11.1 to 20.7)	4.5
Mechanical ventilation	490/5406	12.2 (9.7 to 15.3)	15.5
Inotropes	354/3856	11.8 (8.3 to 16.4)	11.5
Antimalarial	336/3299	9.9 (6.9 to 14.0)	0.0
Aspirin	238/2588	9.0 (5.9 to 13.6)	78.1
Interferon	138/2598	7.7 (4.9 to 11.8)	0.0
Traditional medicine	22/4229	4.0 (2.8 to 5.6)	38.7
Clinical outcomes			
Recovered	8704/9335	88.9 (86.0 to 91.2)	36.3
ICU admission	1359/9335	22.9 (17.6 to 29.2)	37.2
Deaths	96/6902	3.6 (2.8 to 4.5)	24.3

ICU, intensive care unit; IVIG, intravenous immunoglobulin.

Table 4 Comparison of clinical symptoms, management and outcomes among reported paediatric COVID-19 non-severe (n=2402 cases, 64 studies) and severe (n=796 cases, 38 studies) cases

Characteristics	Non-severe cases		Severe cases		RR severe vs non-severe (95% CI)
	Events/total patients	Mean proportion % (95% CI)	Events/total patients	Mean proportion % (95% CI)	
Clinical symptoms					
Fever	1394/2404	51.4 (45.7 to 57.0)	608/756	80.2 (73.6 to 85.5)	1.39 (1.32 to 1.46)
Pharyngeal erythema	541/1149	8.6 (5.1 to 14.0)	41/585	8.8 (5.1 to 14.8)	0.15 (0.11 to 0.20)
Cough	587/1521	35.1 (29.2 to 41.5)	225/618	34.0 (24.6 to 44.9)	0.94 (0.84 to 1.07)
Comorbidity	541/2283	19.8 (14.5 to 26.4)	351/764	44.1 (34.9 to 53.8)	1.94 (1.74 to 2.16)
Nausea/vomiting	206/1291	12.1 (8.7 to 16.6)	224/632	41.0 (36.7 to 45.5)	2.27 (1.93 to 2.67)
Dyspnoea	260/1646	12.7 (9.5 to 16.8)	237/701	36.4 (26.5 to 47.5)	2.14 (1.84 to 2.49)
Nasal symptoms	402/1659	14.1 (9.9 to 19.7)	91/652	15.8 (10.6 to 23.0)	0.58 (0.47 to 0.71)
Fatigue	192/1319	13.8 (10.4 to 18.0)	151/505	20.3 (15.3 to 33.4)	2.05 (1.70 to 2.48)
Kawasaki shock/sign	135/1243	8.5 (5.6 to 12.6)	242/695	30.7 (19.3 to 45.0)	3.21 (2.65 to 3.87)
Rashes	168/1587	10.3 (7.6 to 13.7)	180/660	32.3 (22.3 to 44.2)	2.58 (2.13 to 3.11)
Abdominal pain	95/1193	8.1 (5.8 to 11.3)	184/621	28.4 (18.8 to 40.4)	3.72 (2.96 to 4.67)
Diarrhoea	144/1326	13.5 (10.6 to 17.1)	217/632	35.3 (26.3 to 45.4)	3.16 (2.62 to 3.82)
Conjunctivitis	111/1621	7.5 (5.1 to 10.8)	116/657	22.6 (15.1 to 32.4)	2.58 (2.02 to 3.29)
Neurological symptoms	200/2230	11.0 (9.0 to 13.4)	118/703	17.4 (11.9 to 24.6)	1.87 (1.52 to 2.31)
Clinical management					
Mechanical ventilation	–	–	322/735	43.8 (33.8 to 54.3)	–
Antiviral	217/715	26.5 (17.5 to 38.1)	136/567	24.1 (16.2 to 34.3)	0.79 (0.66 to 0.95)
Interferon	127/685	20.2 (11.6 to 32.3)	4/445	6.8 (3.6 to 12.3)	0.05 (0.02 to 0.13)
Antibiotics	180/363	21.6 (14.2 to 31.3)	365/566	59.6 (44.3 to 73.3)	1.30 (1.15 to 1.47)
Antimalarial	73/717	10.1 (6.4 to 16.4)	123/537	22.9 (14.3 to 34.6)	2.25 (1.72 to 2.94)
IVIg	54/721	11.8 (7.2 to 18.8)	202/498	41.1 (27.0 to 56.8)	5.42 (4.10 to 7.15)
Systemic steroids	46/721	8.9 (5.4 to 14.4)	265/575	46.8 (35.7 to 58.2)	7.22 (5.39 to 9.69)
Inotropes	24/718	6.8 (4.1 to 11.7)	171/498	33.6 (21.2 to 48.9)	10.27 (6.81 to 15.50)
Traditional medicine	18/723	7.4 (4.8 to 11.3)	4/575	6.3 (3.8 to 10.3)	0.28 (0.10 to 0.82)
Aspirin	11/683	6.7 (4.3 to 10.4)	83/445	14.9 (7.9 to 26.4)	11.58 (6.25 to 21.47)
Clinical outcomes					
ICU	–	–	793/796	95.0 (92.1 to 96.8)	–
Recovered	1700/1925	85.4 (76.5 to 91.2)	532/796	77.6 (67.5 to 85.3)	0.76 (0.72 to 0.80)
Deaths	0/1925	–	44/796	8.0 (5.2 to 12.1)	–

ICU, intensive care unit; IVIG, intravenous immunoglobulin.

Table 5 Comparison of clinical symptoms, management and outcomes among reported paediatric COVID-19 cases in HICs (n=5641 cases, 60 studies) and LMICs (n=3694, 69 studies)

Characteristics	HICs		LMICs		RR LMICs vs HICs, (95% CI)
	Events/total patients	Mean proportion % (95% CI)	Events/total patients	Mean proportion % (95% CI)	
Clinical symptoms					
Fever	2276/3332	72.0 (66.3 to 77.0)	1300/2964	50.0 (47.4 to 52.6)	0.64 (0.61 to 0.67)
Cough	995/2730	33.2 (27.5 to 39.5)	812/2531	39.2 (36.2 to 42.3)	0.88 (0.82 to 0.95)
Comorbidity	1069/3357	33.7 (27.4 to 38.5)	521/2729	20.8 (18.3 to 23.4)	0.60 (0.55 to 0.66)
Rashes	491/2109	24.9 (17.9 to 33.5)	253/2278	20.2 (17.5 to 23.2)	0.48 (0.41 to 0.55)
Nausea/vomiting	668/2374	30.3 (24.3 to 37.0)	212/1869	15.3 (12.6 to 18.3)	0.40 (0.35 to 0.46)
Conjunctivitis	309/2732	13.1 (8.4 to 20.1)	220/2266	19.5 (16.9 to 22.5)	0.86 (0.73 to 1.01)
Dyspnoea	543/2454	23.6 (18.5 to 29.6)	336/2878	20.6 (18.1 to 23.4)	0.53 (0.47 to 0.60)
Kawasaki shock/sign	583/2087	21.9 (14.1 to 32.5)	238/2278	21.4 (18.5 to 24.6)	0.37 (0.33 to 0.43)
Fatigue	394/1943	16.8 (12.2 to 22.6)	315/2531	15.6 (13.3 to 18.3)	0.61 (0.54 to 0.70)
Abdominal pain	457/2266	22.7 (16.4 to 30.5)	169/1869	16.6 (12.9 to 21.1)	0.45 (0.38 to 0.53)
Nasal symptoms	425/2549	17.8 (14.4 to 21.8)	269/2519	15.4 (13.2 to 17.8)	0.64 (0.56 to 0.74)
Diarrhoea	527/2365	27.5 (21.5 to 34.6)	125/1105	14.7 (12.4 to 17.3)	0.51 (0.42 to 0.61)
Neurological symptoms	493/3197	15.0 (11.6 to 19.0)	200/2278	10.4 (8.8 to 12.3)	0.57 (0.49 to 0.67)
Asymptomatic	263/2428	6.4 (4.2 to 9.7)	851/3656	20.2 (18.4 to 22.1)	2.15 (1.89 to 2.44)
Pharyngeal erythema	73/1494	6.7 (4.3 to 10.1)	519/2531	40.7 (37.4 to 44.0)	4.20 (3.31 to 5.32)
Clinical management					
Antibiotics	908/1875	36.4 (25.6 to 48.7)	437/1735	27.0 (22.9 to 31.5)	0.52 (0.47 to 0.57)
IVIG	504/1867	31.6 (20.3 to 45.5)	194/1655	14.7 (12.1 to 17.7)	0.43 (0.37 to 0.51)
Aspirin	187/985	16.0 (9.1 to 26.8)	51/1603	10.4 (7.2 to 14.7)	0.17 (0.12 to 0.23)
Systemic steroids	566/2523	27.2 (19.0 to 37.3)	235/1706	18.0 (15.2 to 21.2)	0.61 (0.53 to 0.71)
Inotropes	309/2309	19.1 (12.3 to 28.5)	45/1547	11.9 (8.5 to 16.5)	0.22 (0.16 to 0.30)
Antimalarial	241/1696	13.6 (8.7 to 20.8)	95/1603	13.5 (10.5 to 17.3)	0.42 (0.33 to 0.52)
Mechanical ventilation	387/2930	17.2 (13.1 to 22.3)	103/2476	10.8 (8.6 to 13.4)	0.32 (0.26 to 0.39)
Antiviral	230/2372	11.4 (7.7 to 16.6)	297/1647	25.2 (21.1 to 29.9)	1.86 (1.58 to 2.18)
Interferon	0/995	–	138/1603	30.5 (24.1 to 37.7)	–
Traditional medicine	0/2523	–	22/1706	11.3 (8.0 to 15.7)	–
Clinical outcomes					
Recovered	5269/5641	91.0 (87.7 to 93.4)	3435/3694	83.9 (81.2 to 86.2)	0.99 (0.98 to 1.01)
ICU admission	993/5641	26.0 (24.0 to 28.0)	366/3694	9.9 (8.5 to 11.6)	0.56 (0.50 to 0.63)
Deaths	40/4710	2.9 (2.1 to 4.1)	56/2192	5.2 (4.1 to 6.7)	2.14 (1.43 to 3.20)

HICs, high-income countries; ICU, intensive care unit; IVIG, intravenous immunoglobulin; LMICs, low-income and middle-income countries; RR, relative risk.

categorised as non-severe and 44 deaths among severe cases, where disaggregated data were provided. Hospital outcomes were reported for 9335 children; 8704 cases (88.9%, 95% CI 86.0% to 91.2%) were definitively discharged, 96 died and remaining children either remained hospitalised at the time of reporting or were readmitted.

COMPARISON OF OUTCOMES ACCORDING TO WORLD BANK COUNTRY CLASSIFICATION

Of the included studies that reported clinical characteristics and outcomes, 60 studies were from HICs (n=6528) and 69 studies from LMICs (n=3723) as show in table 5. Studies in LMICs included a higher proportion of hospitalised children (1981/3723, 53.2%) compared with HIC studies (2897/6528, 44.4%). Abdominal symptoms and symptoms consistent with MIS-C were more frequently reported in HICs. A lower proportion of children in LMICs were admitted to the ICU (RR 0.56, 95% CI 0.50 to 0.63, $p<0.05$), mechanically ventilated (RR 0.32, 95% CI 0.26 to 0.39, $p<0.05$) and treated with different

therapies; inotropes, antimicrobials, steroids, aspirin and IVIG. Only children in LMICs received inhaled IFN- α . Among the hospitalised cases, 40 deaths were reported in HICs compared with 56 in LMICs (pooled proportion 2.9% vs 5.2%). Risk-adjusted mortality according to severity of illness could not be calculated due to lack of data (table 5).

SUBGROUP ANALYSES OF CHILDREN PRESENTING WITH MIS-C, AND COVID-19 IN NEONATES

Thirty-one studies (n=1208) with 22 from HIC (n=602), reported series of children presenting with MIS-C. Fever, abdominal pain and diarrhoea were the most common symptoms. Nearly half of children (638/1208) who met criteria for MIS-C were admitted to ICU (449/638, 70.3% of which were from HIC) compared with 22.9% in the overall analysis (online supplemental tables 6 and 7).

Disaggregated data were available on 184 neonates with fever; inability to feed/lethargy and dyspnoea were the most commonly

reported symptoms. Twenty-one neonates (16.6%, 95% CI 11.2% to 23.9%) were asymptomatic at the time of diagnosis.

QUALITY ASSESSMENT OF INCLUDED STUDIES

One hundred and twenty-one studies were determined to be of good quality while eight were of fair quality (online supplemental table 8). Studies were primarily downgraded for incomplete case definition,^{29 31 44 46 48–50 130 135 138} incomplete case follow-up,^{10 23 24 26 29 32 35 44 51 53 77 82 85 90 94 99 106 112–114 120 130 135–137} missing data^{2 3 19–21 29 35 42–44 52 57 74 89 92–94 117 128} and non-consecutive patient enrolment,^{9 11 12 16 18–26 28 30–35 37–39 50 57 61–73 80 82 87 89–91 93 95 102 109 110 112 114 123 125 126 129 134–136} which raises concern that the included sample could be biased towards more severe presentations.

DISCUSSION

Global knowledge of COVID-19 epidemiology, clinical characteristics and management has continued to evolve since the onset of the pandemic. Children have been noted to have relatively lower rates of severe illness and low mortality; however, they have been impacted by MIS-C.^{4 139}

The findings of our review, the largest in terms of published systematic reviews on paediatric COVID-19, are consistent with previous reviews that identified predominance of infection in school-age children, slight male predisposition, prevalence of comorbidities among children with COVID-19 and low hospitalisation and mortality rates.^{2 4 140} The clinical presentation in children is heterogeneous, including a wide spectrum of clinical features. Fever and cough were the most commonly reported presenting symptoms, in line with the previously published systematic reviews.^{4 141} A U-shaped curve of severity has been demonstrated in children diagnosed with COVID-19 with infants under 1 year of age and adolescents 10–14 years of age at higher risk of developing severe COVID-19.^{3 47 75} Due to lack of age-disaggregated data, we could not reliably compare the frequency of severe cases by age group in this review. Reported risk factors for severe disease among children include age, viral load¹⁴² and presence of comorbidities.³ There is a possibility that children with comorbidities may have been hospitalised related to their underlying chronic condition and incidentally determined to have COVID-19 infection or investigated more extensively. Some of the common comorbidities reported in children with COVID-19 infection include asthma, immunosuppression, congenital heart disease, kidney disease and obesity.^{3 4 47}

Regional differences were identified in the comparison of clinical features, treatment and outcomes between HICs and LMICs. Pooled estimates of hospital mortality were higher in LMICs compared with HICs. Given that it was not possible to calculate risk-adjusted mortality rates for COVID-19, it is unclear whether observed differences in mortality are related to selection bias (eg, differences in severity of illness of included patients or differences in case definitions and inclusion criteria) or differences in available hospital resources. Nevertheless, there is ongoing concern that, in LMICs with high burden of illness and health system limitations, children with severe disease and MIS-C may be at greater risk for adverse outcomes and death than perceived to date. The differences in frequency of observed clinical features may be related to increasing recognition of MIS-C over the course of the pandemic and their inclusion in more recent COVID-19 case series, but is likely similar between HICs and LMICs.

Comparisons of clinical features and outcomes according to severity of illness were limited by heterogeneous reporting

across the included case series. A higher proportion of children with severe disease demonstrated symptoms consistent with MIS-C (fever, abdominal symptoms, rash, neurological symptoms, conjunctivitis) and received IVIG, steroids and inotropes.

Compared with previous reviews, several at an earlier stage of the pandemic,^{4 7 8 140 143} this review has several strengths. Using a broad search strategy implemented in English, Chinese and Spanish databases, we summarise evidence from 129 studies from 31 different countries, the largest sample to-date. We excluded case reports to minimise selective reporting of extreme and atypical cases. We also attempted to reduce possible overlap in cases to prevent duplications. We identified differences in features from studies in HICs compared with LMICs, and between severe and non-severe cases, although with limited available data. Finally, we report subgroup analyses for neonates, and children presenting with MIS-C.

The review is limited primarily by the small sample sizes of individual studies, limitations in study reporting, and study quality limitations due to non-consecutive patient enrolment, unclear case definition and incomplete follow-up to hospital discharge. Our approach of pooling proportions is subject to bias and wide confidence-intervals due to small study sample size. We could not undertake multivariate analysis to identify risk factors for severe infection or adverse outcome in children due to lack of individual-patient-data. The inclusion of asymptomatic cases could have contributed to underestimation of the prevalence of clinical characteristics and optimism in the reporting of outcomes. Finally, it should be noted that a large number (36/129, 28.0%) of the included studies were from China. While the Chinese healthcare system is well-resourced in certain regions, many of the Chinese studies included were conducted in the city of Wuhan or in Hubei Province (n=9, 32.1%), where the gross domestic product per capita is less than half of that of Beijing and Shanghai.¹⁴⁴ Therefore, the findings of studies from China may be generalisable to the socioeconomic and health development status of other middle-income countries.

This review contributes to the global understanding of paediatric COVID-19 disease and supports priority setting in research for current pandemic and future outbreaks. This body of literature would be improved by complete reporting of larger series with consecutive recruitment of patients, specific case definitions and complete long-term follow-up to determine global epidemiological trends, age-specific burden of disease and illness trajectory following COVID-19 infection. Improved characterisation of disease severity and increased reports from low-income countries are needed to better understand differences in clinical manifestations, resource utilisation and outcome by region, which can be integrated in future updated analyses. The concern for selection bias remains as it is possible that in LMICs, the population of hospitalised children was sicker and at higher baseline risk of death, independent of resources. Individual-patient-data meta-analysis would be of benefit to characterise risk factors for severe disease, clinical features in different age groups and account for observed differences in outcome. With respect to clinical management, none of the therapies instituted in the treatment of children with severe COVID-19 disease have been demonstrated to improve outcome in randomised trials; therefore, a recommendation regarding their use is challenging. Given that children appear less likely to develop severe respiratory disease, but are at risk of multiorgan dysfunction due to MIS-C, further studies are needed to characterise the clinical trajectory of this novel syndrome and determine the optimal treatment for it. Finally, there remains paucity of studies reporting long-term prognosis of COVID-19 in children.¹⁴⁵

CONCLUSION

Our review suggests that children predominantly contracted mild form of infection but could be at risk of more severe outcomes. It is crucial to take into consideration risk factors including contact-exposure, underlying comorbidities, young age and male sex which may increase the risk of severe disease. While we have identified several elements that highlight the disease spectrum and higher risk of adverse outcomes in certain settings, such as LMICs, there is the need for much closer scrutiny of this illness globally with individual patient data analysis.

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Clinical characteristics, treatment and outcomes of pediatric COVID-19: a systematic review and meta-analysis**Supplement file**

Table 1: Search Strategy for MEDLINE

Table 2: Distribution of studies (N=129) according to Country of origin included in the review

Table 3: Characteristics of included studies (N=129)

Table 4: Age Distribution from 91 studies of disease prevalence

Table 5: Age Distribution from 67 case series of clinical features and outcomes

Table 6: Characteristics of included studies with MIS-C

Table 7: Characteristics of included studies from neonatal age group

Table 8: Quality assessment of included studies (N=129)

Figure 1: Flow diagram of the systematic review process

Figure 2: Global map of distribution of the studies included (N=129) in the review

Table 1: Search Strategy for MEDLINE

- 1- (coronavirus or "covid 2019" or "SARS2" or "SARS" or "SARS CoV19" or "severe acute respiratory syndrome coronavirus 2" or "coronavirus infection" or "severe acute respiratory pneumonia outbreak" or "novel cov" or 2019ncov or sars cov2 or cov2 or ncov or covid or covid19 or coronaviridae or "corona virus").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 2- "coronavirus infections".mp. or exp Coronavirus Infections/
- 3- exp Coronavirus 229E, Human/ or exp Coronavirus/ or exp Middle East Respiratory Syndrome Coronavirus/ or coronavirus.mp.
- 4- 1 or 2 or 3
- 5- (infant or neonate or newborn or child or children or pediatric* or paediatric or baby or babies or toddler).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 6- exp Infant, Low Birth Weight/ or exp Infant, Extremely Premature/ or exp Infant/ or exp Infant, Newborn/ or exp Infant, Premature/
- 7- 5 or 6
- 8- 4 and 7

Table 2: Distribution of studies (N=129) according to Country of origin included in the review

Country	Count of reports	Sum of COVID-19 cases
USA	24	3443
China	36	1315
Canada	1	938
UK	9	867
Kazakhstan	1	650
25 European Countries	1	582
Italy	4	171
Spain	8	287
Korea	1	91
India	5	145
Turkey	3	338
Jordan	1	61
France	4	47
Iran	7	152
Brunei-Darussalam	1	12
Chile	1	27
Bangladesh	1	26
Brazil	4	261
Pakistan	3	20
Poland	1	9
Kuwait	1	134
Saudi Arabia	1	10
Australia	1	4
Malaysia	1	4
Romania	1	3
Japan	1	3
Germany	1	3
Mexico	2	53
South Africa	2	182
Peru	1	69
5 Latin American Countries (Mexico, Colombia, Peru, Costa Rico, Brazil)	1	409

Total

129

10251

Table 3: Characteristics of included studies (N=129)

Study and year	Country	World Bank Country Classification	Total number (N)	Study setting	Mean age (years)	Males (N)	Past medical history and Contact history	Presenting signs and symptoms	Management (other than supportive care)	Outcomes
Qiu, H 2020	China	LMIC	36	Patients presenting to hospital	8.3	23	Travel history (n=12) Contact history (n=32) Comorbidities (NR)	Fever (n=13), cough (n=7), headache (n=3), nasal symptoms (n=2), GI symptoms (n=2)	Interferon (n=36), antivirals (n=14), oxygen (n=6)	Recovered (n=36) ICU admission (n=0)
Wang, D 2020	China	LMIC	31	Patients admitted in hospital	7.1	15	Travel history (n=9) Contact history (n=1) Comorbidities (n=0)	Asymptomatic (n=7), fever (n=20), cough (n=14), fatigue and diarrhea (n=3 each), sore throat (n=2), headache/dizziness (n=3), rhinorrhoea (n=2), vomiting (n=2)	Interferon (n=10), Antibiotics (n=6), antivirals (n=29), traditional medicine (n=9), IVIG (n=4)	Recovered (n=24) ICU admission (n=0)
Zheng, F 2020	China	LMIC	25	Patients admitted in hospital	3.0	14	Travel history (n=9) Contact history (n=1) Comorbidities (n=0)	Fever (n=13), cough (n=11), diarrhea (n=3), dyspnea (n=2), vomiting (n=2), abdominal pain (n=2), nasal congestion (n=2)	Interferon (n=2), Antibiotics (n=2), antivirals (n=2), steroids (n=2), IVIG (n=4), Mechanical ventilation (n=2)	Recovered (NR) ICU admission (n=2)

Xia, W 2020	China	LMIC	20	Patients admitted in hospital	4.8	13	Travel history (n=20) Contact history (n=13) Comorbidities (NR)	Cough (n=13), fever (n=12), diarrhea (n=3), dyspnea (n=2), sore throat (n=1), fatigue (n=1)	NR	Recovered (n=19) ICU admission (n=1)
Feng, K 2020	China	LMIC	15	Patients presenting to hospital	NR	5	Travel history (n=3) Contact history (n=12) Comorbidities (NR)	Asymptomatic (n=8), fever (n=5), cough or nasal congestion (n=1)	NR	Recovered (n=5) ICU admission (n=0)
Cai, J 2020	China	LMIC	10	Patients admitted in hospital	6.5	4	NR	Fever (n=8), cough (n=6) or sore throat or nasal congestion (n=7)	Antibiotics (n=5)	Recovered (n=10) ICU admission (n=0)
Wei, M 2020	China	LMIC	9	Patients admitted in hospital	0.5	2	Travel history (n=7) Contact history (n=9) Comorbidities (NR)	Asymptomatic (n=6), fever (n=4), cough (n=2), rhinorrhoea (n=1), sputum production (n=1)	NR	Recovered (n=9) ICU admission (n=0)
Su, L 2020	China	LMIC	9	Patients presenting to hospital	4.5	3	Travel history (n=8) Contact history (n=9) Comorbidities (NR)	Asymptomatic (n=6), fever or cough (n=3)	Interferon given to all patients; antivirals (n=2)	Recovered (NR) ICU admission (n=0)
Zhou, Y 2020	China	LMIC	9	Patients admitted in hospital	1.0	4	Travel history (n=3) Contact history (n=9) Comorbidities (n=0)	Asymptomatic (n=5), fever (n=4), cough (n=2), rhinorrhoea (n=1)	Interferon (n=9) antivirals (n=6), mechanical ventilation (n=9)	Recovered (NR) ICU admission (n=0)
Sun, D 2020	China		8		6.8	6	Travel history (n=8)	Fever or cough (n=6 each), sputum production (n=4),	mechanical ventilation (n=2), antibiotics (n=5),	Recovered (n=5)

		LMIC		Patients admitted in hospital			Contact history (n=5) Comorbidities (n=3)	nausea/ vomiting (n=4), diarrhea (n=3), fatigue (n=1) or headache (n=1), sore throat or nasal symptoms (n=8)	systemic steroids (n=5), IVIG (n=4), Chinese medications (n=4)	ICU admission (n=8)
Liu, W 2020	China	LMIC	6	Patients admitted in hospital	3.0	2	NR	High fever and cough in all patients; vomiting and fatigue (n=4)	Antivirals (n=6), systemic steroids (n=4), IVIG (n=1)	Recovered (n=5) ICU admission (n=1)
Hu, Z 2020	China	LMIC	7	Patients admitted in hospital	8.0	5	Travel history (n=3) Contact history (n=0) Comorbidities (NR)	Asymptomatic (n=4), fever (n=1)	NR	Recovered (n=6) ICU admission (NR)
Liu, M 2020	China	LMIC	5	Patients admitted in hospital	5.9	4	Travel history (n=0) Contact history (n=5) Comorbidities (NR)	Fever (n=2), cough (n=2), diarrhea (n=1), asymptomatic (n=3)	Antiviral (n=3), Interferon (n=4)	Recovered (n=5) ICU admission (n=0)
Liu, H 2020	China	LMIC	4	Patients presenting to hospital	3.0	2	Travel history (n=4) Contact history (n=4) Comorbidities (NR)	Fever (n=3), cough (n=3), Fatigue (n=1)	NR	NR
Lou, MX 2020	China	LMIC	3	Patients admitted in hospital	4.8	1	Travel history (n=2) Contact history (n=3) Comorbidities (NR)	Fever (n=3), cough (n=1), Fatigue (n=2), diarrhea (n=2), nasal symptoms or sore throat (n=2)	Antibiotics (n=1), interferon (n=2)	Recovered (n=3) ICU admission (n=0)
Zhang, T 2020	China	LMIC	3	Patients admitted in hospital	7.7	3	Travel history (n=0) Contact history (n=3)	Fever (n=2), cough (n=1), Fatigue (n=1), nausea or vomiting (n=2), nasal symptoms or sore throat (n=3)	Antibiotics (n=1), antivirals (n=1), interferon (n=3), Chinese medicine (n=3)	Recovered (n=3) ICU admission (NR)

							Comorbidities (NR)			
Li, Y 2020	China	LMIC	2	Patients admitted in hospital	4.0	1	Travel history (n=2) Contact history (n=2) Comorbidities (n=0)	Cough (n=1), nasal symptoms (n=1), asymptomatic (n=1)	NR	Recovered (NR) ICU admission (NR)
Ji, LN 2020	China	LMIC	2	Patients admitted in hospital	12.0	2	Travel history (n=2) Contact history (n=2) Comorbidities (n=0)	Fever (n=1), nasal symptoms (n=1), sore throat (n=1)	NR	Recovered (NR) ICU admission (n=0)
Tagarro, A 2020	Spain	HIC	41	Patients admitted in hospital	4.3	18	Travel history (NR) Contact history (n=16) Comorbidities (n=2)	Upper respiratory symptoms in 14 (34%), fever (n=11), gastroenteritis or vomiting (n=2)	Mechanical ventilation (n=4)	Recovered (n=37) ICU admission (n=4)
Chen, A 2020	China	LMIC	14	Patients admitted in hospital	4.3	8	Travel history (n=10) Contact history (n=4) Comorbidities (n=0)	Fever (n=6), cough (n=6), Fatigue (n=3), nasal symptoms or sore throat (n=2)	NR	NR
See, KC 2020	Malaysia	LMIC	4	Patients presenting to hospital	6.4	3	Travel history (n=4) Contact history (n=0) Comorbidities (N=1)	Fever (n=1), cough (n=2), diarrhea (n=1), asymptomatic (n=2)	Antibiotics (n=1)	Recovered (n=4) ICU admission (n=0)
Zhang, GX 2020	China	LMIC	2	Patients admitted in hospital	1.2	0	Travel history (n=0) Contact history (n=2)	Fever (n=2), fatigue (n=1), dyspnea (n=1), diarrhea (n=2), nausea or vomiting (n=2),	IVIg (n=1), interferon (n=2), Chinese medicine (n=1)	Recovered (n=2) ICU admission (n=0)

							Comorbidities (n=0)			
Cheng, X 2020	China	LMIC	2	Patients admitted in hospital	1.0	1	Travel history (n=2) Contact history (n=0) Comorbidities (n=0)	Fever (n=2), fatigue (n=1), dyspnea (n=1), diarrhea (n=2), nausea or vomiting (n=2),	Antibiotics (n=2), interferon (n=1), Chinese medicine (n=1)	Recovered (n=2) ICU admission (n=1)
Tang, A 2020	China	LMIC	26	Patients admitted in hospital	6.9	17	Travel history (n=26) Contact history (n=26) Comorbidities (n=0)	Fever (n=11), cough (n=12), diarrhea (n=2), nausea or vomiting (n=2), nasal symptoms or sore throat (n=2), asymptomatic (n=9)	Antivirals (n=22), interferon (n=4)	Recovered (n=17) ICU admission (n=0)
Zhu, L 2020	China	LMIC	10	Patients admitted in hospital	9.1	1	Travel history (n=8) Contact history (n=10) Comorbidities (n=0)	Fever (n=3), cough (n=3), asymptomatic (n=6)	Antivirals (n=1), interferon (n=10)	Recovered (n=10) ICU admission (n=0)
Tan, X 2020	China	LMIC	13	Patients admitted in hospital	7.9	4	Travel history (n=3) Contact history (n=10) Comorbidities (n=0)	Fever (n=6), cough (n=6), nasal symptoms (n=1), diarrhea (n=1), nausea or vomiting (n=1), abdominal pain (n=1), headache (n=1), asymptomatic (n=2)	Antivirals (n=12), interferon (n=10)	Recovered (n=13) ICU admission (n=0)
Ma, H 2020	China	LMIC	22	Patients admitted in hospital	5.5	12	Travel history (n=22) Contact history (n=0) Comorbidities (n=0)	Fever (n=13), dry cough (n=5), shortness of breath (n=1), asymptomatic (n=2)	NR	Recovered (n=5) ICU admission (n=0)
Shen, Q 2020	China	LMIC	9	Patients admitted in hospital	7.6	3	Travel history (n=2) Contact history (n=6)	asymptomatic (n=2), fever (n=3), diarrhea (n=2), sore throat (n=1), cough (n=1)	Antivirals (n=9), antibiotics (n=4), IVIG (n=1), Systemic steroids (n=1)	Recovered (n=6) ICU admission (n=0)

							Comorbidities (n=0)			
Schwierz eck, V 2020	Germany	HIC	3	Patients admitted in hospital	10.0	NR	Travel history (n=0) Contact history (NR) Comorbidities (n=3)	Asymptomatic (n=2), fever (n=1), cough (n=1), nasal congestion (n=1)	NR	NR
Jiang, JY 2020	China	LMIC	6	Patients presenting to hospital	7.0	5	Travel history (n=0) Contact history (n=6) Comorbidities (NR)	Fever (n=3), cough (n=2), diarrhea (n=3), asymptomatic (n=3)	NR	Recovered (n=6) ICU admission (n=0)
Riphagen , S 2020	UK	HIC	8	Patients admitted in hospital	8.9	5	Travel history (NR) Contact history (NR) Comorbidities (NR)	Fever (n=8), diarrhea (n=7), rashes (n=4), conjunctivitis (n=5)	IVIG (n=6), Systemic steroids (n=5), Inotropes (n=8), aspirin (n=3)	Recovered (n=7) ICU admission (n=8) Death (n=1)
Shekerde mian, LS 2020	USA	HIC	48	Patients admitted to intensive care units	11.7	25	Travel history (NR) Contact history (NR) Comorbidities (n=40)	Multi-organ failure (n=11), pulmonary symptoms (n=35), diarrhea (n=1), headache (n=2), asymptomatic (n=1)	hydroxychloroquine (n=21), antiviral (n=8), mechanical ventilation (n=18), antibiotics (n=15)	Recovered (n=31) ICU admission (n=48) Death (n=2)
Verdoni, L 2020	Italy	HIC	10	Patients admitted in hospital	7.5	7	Travel history (NR) Contact history (NR) Comorbidities (n=5)	GI symptoms (n=5), neurological (n=4), Kawasaki signs (n=12), rashes (n=5)	IVIG (n=8), Inotropes (n=2)	Recovered (n=10) ICU admission (n=0)
Rahimza deh, G 2020	Iran	LMIC	9	Patients admitted in hospital	4.9	6	Travel history (n=0) Contact history (n=0)	Fever (n=9), cough (n=9), fatigue (n=9), asymptomatic (n=3)	Mechanical ventilation (n=2), antivirals (n=9), antibiotics (n=9), antimalarials (n=9)	Recovered (n=9) ICU admission (n=2)

							Comorbidities (n=0)			
Tullie, L 2020	UK	HIC	8	Patients admitted in hospital	NR	NR	NR	Fever (n=8), Kawasaki signs (n=4), rashes (n=4), GI symptoms (n=8)	antibiotics (n=8), IVIG (n=4)	Recovered (n=7) ICU admission (n=4)
Sajid, MI 2020	Pakistan	LMIC	2	Patients admitted in hospital	12.0	1	Travel history (NR) Contact history (NR) Comorbidities (n=2)	Fever (n=2), cough (n=1)	NR	Recovered (NR) ICU admission (n=0)
Zhang, ZJ 2020	China	LMIC	4	Patients admitted in hospital	Newborns	3	Travel history (NR) Contact history (NR) Comorbidities (n=2)	Fever (n=2), shortness of breath (n=1), cough (n=1), vomiting (n=1), asymptomatic (n=1)	NR	Recovered (NR) ICU admission (n=0)
Zeng, L 2020	China	LMIC	3	Patients admitted in hospital	Newborns	3	Travel history (n=3) Contact history (n=3) Comorbidities (n=0)	Fever (n=2), cough (n=1), fatigue (n=1)	Mechanical ventilation (n=1), antibiotics (n=1)	Recovered (NR) ICU admission (n=3)
Salvatori, G 2020	Italy	HIC	2	Patients presenting to hospital	Newborns	1	Travel history (NR) Contact history (NR) Comorbidities (n=0)	Cough (n=1), fatigue (n=1), diarrhea (n=1), asymptomatic (n=1)	NR	Recovered (n=2) ICU admission (n=0)
Zhang, X 2020	China	LMIC	10	Patients presenting to hospital	4.9	3	Travel history (n=0) Contact history (n=10) Comorbidities (n=0)	Fever (n=3), Cough (n=1), sore throat (n=1), asymptomatic (n=5)	NR	Recovered (n=10) ICU admission (n=0)
Wu, HP 2020	China		23		NR	NR	Travel history (n=7)	Fever (n=16), Cough (n=11), diarrhea (n=2),	Antivirals (n=8), antibiotics (n=6),	Recovered (n=23) ICU admission (n=0)

		LMIC		Patients admitted in hospital			Contact history (n=17) Comorbidities (n=0)	sore throat (n=2), asymptomatic (n=3)	interferon (n=17), antimalarial (n=1)	
Zhang, H 2020	China	LMIC	2	Patients presenting to hospital	13.5	2	Travel history (n=2) Contact history (n=2) Comorbidities (n=2)	Fever (n=1), Cough (n=1), asymptomatic (n=1)	Antivirals (n=2), antibiotics (n=1), interferon (n=2)	Recovered (n=2) ICU admission (n=0)
Chao, JY 2020	USA	HIC	46	Patients admitted in hospital	13.1	31	Travel history (n=0) Contact history (n=20) Comorbidities (n=31)	Fever (n=28), Cough (n=28), dyspnea (n=22) asymptomatic (n=1)	NR	Recovered (n=45) ICU admission (n=13) Deaths (n=1)
Eghbali, A 2020	Iran	LMIC	4	Patients admitted in hospital	11.0	4	Travel history (NR) Contact history (NR) Comorbidities (n=2)	Fever (n=4), Cough (n=4), dyspnea (n=2)	Mechanical ventilation (n=2)	Recovered (n=4) ICU admission (n=2)
Chiotos, K 2020	USA	HIC	6	Patients admitted in hospital	8.5	1	Travel history (n=0) Contact history (n=0) Comorbidities (n=0)	Fever (n=6), diarrhea (n=6), nausea of vomiting (n=5), abdominal pain (n=5), dyspnea (n=4), kawasaki signs (n=6), rashes (n=2), conjunctivitis (n=2)	IVIG (N=6), Systemic steroids (n=3), inotropes (n=6), aspirin (n=3)	Recovered (n=5) ICU admission (n=1)
Flores, V 2020	Mexico	LMIC	3	Patients admitted in hospital	7.0	0	Travel history (NR) Contact history (n=0) Comorbidities (n=3)	Fever (n=3), dyspnea (n=1)	Mechanical ventilation (n=1), Antibiotics (n=3)	Recovered (n=2) ICU admission (n=1) Deaths (n=1)
García-Salido, A 2020	Spain		7	Patients admitted in hospital	8.4	4	Travel history (NR)	Fever (n=5), dyspnea (n=3), diarrhea (n=3), nausea or vomiting (n=3)	Antivirals (n=6), antibiotics (n=6), IVIG	Recovered (n=7) ICU admission (n=7)

		HIC		Patients admitted to intensive care units			Contact history (NR) Comorbidities (n=1)		(n=2), systemic steroids (n=6), antimalarial (n=6), interferon (n=2)	
Cabrero-Hernández, M 2020	Spain	HIC	5	Patients admitted to intensive care units	10.6	4	Travel history (NR) Contact history (NR) Comorbidities (n=0)	Fever (n=5), diarrhea (n=3), nausea or vomiting (n=2), abdominal pain (n=5), Kawasaki signs (n=1), rashes (n=1)	Mechanical ventilation (n=5), Systemic steroids (n=5), antimalarial (n=5), inotropes (n=4)	Recovered (n=5) ICU admission (n=5)
Waltuch, T 2020	USA	HIC	4	Patients admitted to intensive care units	10.0	3	Travel history (n=0) Contact history (n=2) Comorbidities (n=2)	Fever (n=4), Cough (n=2), fatigue (n=2), GI symptoms (n=3), Kawasaki signs (n=2), rashes (n=2), conjunctivitis (n=1)	Antibiotics (n=4), IVIG (n=2), Inotropes (n=1)	Recovered (n=4) ICU admission (n=4)
Kakuya, F 2020	Japan	HIC	3	Patients presenting to hospital	8.3	3	Travel history (n=0) Contact history (n=1) Comorbidities (n=0)	Fever (n=3), Cough (n=3), fatigue (n=1),	Antibiotics (n=2)	Recovered (n=3) ICU admission (n=0)
Soltani, J 2020	Iran	LMIC	30	Patients presenting to hospital	6.0	14	Travel history (NR) Contact history (NR) Comorbidities (n=11)	Fever (n=23), Cough (n=16), dyspnea (n=20), diarrhea (n=3), nausea or vomiting (n=8), nasal symptoms or sore throat (n=6)	Antivirals (n=19), antibiotics (n=17), IVIG (n=2), antimalarial (n=23)	Recovered (n=29) ICU admission (n=1) Deaths (n=1)
Toubiana, J 2020	France	HIC	21	Patients admitted in hospital	7.9	9	Travel history (NR) Contact history (NR) Comorbidities (n=0)	Fever (n=11), GI Symptoms (n=21), neurological (n=6), kawasaki signs (n=11), rashes (n=16), conjunctivitis (n=17)	Mechanical ventilation (n=11), Antibiotics (n=18), IVIG (N=21), Systemic steroids (n=10), Inotropes (n=15), aspirin (n=21)	Recovered (n=21) ICU admission (n=17)
Foster, CE 2020	USA	HIC	57	Patients presenting to hospital	10.6	31	Travel history (n=3) Contact history (n=30)	Fever (n=35), cough (n=34), GI Symptoms (n=21), sore throat or	Antibiotics (n=3), systemic steroids (n=3), IVIG (n=1),	Recovered (n=57) ICU admission (n=0)

							Comorbidities (n=21)	nasal symptoms (n=16), asymptomatic (n=3)		
White, A 2020	USA	HIC	3	Patients admitted in hospital	0.1	2	Travel history (n=0) Contact history (n=2) Comorbidities (n=0)	Fever (n=3), dyspnea (n=3), nasal symptoms (n=3)	NR	Recovered (n=3) ICU admission (n=3)
Lin, EE 2020	USA	HIC	12	Patients admitted in hospital	11.3	8	Travel history (n=0) Contact history (n=2) Comorbidities (n=0)	Fever (n=3), cough (n=1), GI Symptoms (n=1), sore throat (n=2),	NR	Recovered (NR) ICU admission (n=0)
Gao, Y 2020	China	LMIC	11	Patients presenting to hospital	10.3	6	Travel history (n=0) Contact history (n=10) Comorbidities (n=0)	Fever (n=2), cough (n=2), dyspnea (n=1), asymptomatic (n=8)	Antiviral (n=4), interferon (n=7), Chinese medicine (n=5)	Recovered (n=11) ICU admission (n=0)
Harman, K 2020	UK	HIC	5	Patients admitted in hospital	7.1	2	Travel history (NR) Contact history (NR) Comorbidities (n=5)	Fever (n=3), asymptomatic (n=2)	Antiviral (n=1), antibiotics (n=5), antimalarial (n=1)	Recovered (n=4) ICU admission (n=2)
Blondiaux, E 2020	France	HIC	4	Patients admitted in hospital	9.0	1	Travel history (NR) Contact history (n=3) Comorbidities (n=0)	Fever (n=4), GI symptoms (n=4), rashes (n=4), conjunctivitis (n=3)	Mechanical ventilation (n=1), systemic steroids (n=3), inotropes (n=3), aspirin (n=3), IVIG (N=4)	Recovered (n=4) ICU admission (n=4)
Pouletty, M 2020	France	HIC	16	Patients admitted in hospital	10.0	8	Travel history (n=0) Contact history (n=12)	Fever (n=16), cough (n=2), dyspnea (n=2), GI symptoms (n=13), neurological (n=9), Kawasaki signs (n=7),	Mechanical ventilation (n=2), systemic steroids (n=4), antimalarial (n=1), aspirin (n=3), IVIG	Recovered (n=16) ICU admission (n=6)

							Comorbidities (n=6)	rashes (n=13), conjunctivitis (n=15)	(N=15), inotropes (n=6), aspirin (n=15)	
Whittaker, E 2020	UK	HIC	45	Patients admitted in hospital	10.0	19	Travel history (NR) Contact history (NR) Comorbidities (n=7)	Fever (n=45), dyspnea (n=9), GI symptoms (n=25), neurological (n=5), Kawasaki signs (n=25), rashes (n=21), conjunctivitis (n=20)	Mechanical ventilation (n=20), systemic steroids (n=33), IVIG (N=33), inotropes (n=23)	Recovered (n=44) ICU admission (n=20) Death (n=1)
Cheung, EW 2020	USA	HIC	17	Patients admitted in hospital	8.0	8	Travel history (n=0) Contact history (n=11) Comorbidities (n=3)	Fever (n=17), cough (n=7), dyspnea (n=7), neurological (n=8), Kawasaki signs (n=13), rashes (n=12), conjunctivitis (n=11)	Systemic steroids (n=12), IVIG (N=13), inotropes (n=10), aspirin (n=4)	Recovered (n=17) ICU admission (n=15)
Lu, X 2020	China	LMIC	171	National surveillance	6.7	104	Travel history (n=17) Contact history (n=131) Comorbidities (n=9)	Fever (n=71), cough (n=83), pharyngeal erythema (n=79), fatigue (n=13), diarrhea (n=15), nausea or vomiting (n=11), nasal symptoms or sore throat (n=22), asymptomatic (n=27)	NR	Recovered (n=149) ICU admission (n=3) Death (n=1)
CDC, COVID 2020	USA	HIC	2572	National surveillance	9.8	1408	Travel history (n=16) Contact history (n=168) Comorbidities (n=80)	Fever (n=163), cough (n=158), dyspnea (n=39), diarrhea (n=37), nausea or vomiting (n=31), abdominal pain (n=17), nasal symptoms or sore throat (n=71), neurological (n=81)	NR	Recovered (n=2569) ICU admission (n=15) Death (n=3)
Gotzinger, F 2020	Europe	HIC	582	Multinational cohort study	5.6	311	Travel history (n=0) Contact history (n=348) Comorbidities (n=145)	Fever (n=379), GI symptoms (n=128), neurological (n=70), asymptomatic (n=92)	Antiviral (n=30), IVIG (n=7), systemic steroids (n=22), antimalarial (n=40)	Recovered (n=460) ICU admission (n=48) Death (n=4)

Dong, Y 2020	China	LMIC	728	National surveillance study	9.8	418	Travel history (NR) Contact history (NR) Comorbidities (NR)	315 mild illness, 300 moderate illness, 18 severe and 3 critically ill, 94 asymptomatic children	NR	Recovered (n=727) ICU admission (n=21) Death (n=1)
Abdel-Mannan, O 2020	UK	HIC	4	Patients admitted in hospital	11.8	2	Travel history (NR) Contact history (NR) Comorbidities (NR)	Fever (n=4), dyspnea (n=2), nausea or vomiting (n=4), abdominal pain (n=1), neurological (n=4), rashes (n=4)	Mechanical ventilation (n=4), IVIG (n=3), systemic steroids (n=2)	Recovered (n=2) ICU admission (n=4)
Guha, A 2020	India	LMIC	41	National surveillance	1.9	24	Travel history (n=0) Contact history (n=26) Comorbidities (n=25)	Fever (n=9), cough (n=5), dyspnea (n=13), diarrhea (n=3), Kawasaki signs (n=2), rashes (n=2), asymptomatic (n=11)	Mechanical ventilation (n=2)	Recovered (n=40) ICU admission (n=6) Death (n=1)
Bhumbra, S 2020	USA	HIC	19	Patients admitted in hospital	6.7	14	Travel history (NR) Contact history (NR) Comorbidities (n=8)	Fever (n=12), cough (n=5), dyspnea (n=12), nausea or vomiting (n=2), sore throat (n=2),	Mechanical ventilation (n=4)	Recovered (n=12) ICU admission (n=7) Death (n=1)
Bisogno, G 2020	Italy	HIC	29	Patients admitted in hospital	7.5	13	Travel history (NR) Contact history (NR) Comorbidities (n=29)	Fever (n=8), fatigue (n=1), dyspnea (n=7), diarrhea (n=1), nausea or vomiting (n=1), asymptomatic (n=7)	Mechanical ventilation (n=0), antiviral (n=3), antibiotics (n=13), antimalarial (n=9)	Recovered (n=27) ICU admission (n=0)
Blumfield, E 2020	USA	HIC	19	Patients admitted in hospital	8.5	10	Travel history (NR) Contact history (NR)	Fever (n=17), cough (n=13), dyspnea (n=13), diarrhea (n=9), nausea or vomiting (n=9), abdominal pain (n=2),	Mechanical ventilation (n=8)	Recovered (n=17) ICU admission (n=14) Death (n=2)

							Comorbidities (n=12)	neurological (n=5), nasal symptoms or sore throat (n=8)		
Derespin a, KR 2020	USA	HIC	70	Patients admitted in hospital	14.5	43	Travel history (n=2) Contact history (n=30) Comorbidities (n=52)	Fever (n=51), cough (n=50), dyspnea (n=45), fatigue (n=13), diarrhea (n=18), nausea or vomiting (n=24), neurological (n=15), nasal symptoms or sore throat (n=9)	Mechanical ventilation (n=20), antiviral (n=13), antibiotics (n=23), systemic steroids (n=23), antimalarial (n=27), inotropes (n=14)	Recovered (n=55) ICU admission (n=2) Death (n=70)
Feldstein , LR 2020	USA	HIC	186	Patients admitted in hospital	8.1	115	Travel history (NR) Contact history (NR) Comorbidities (n=51)	Fever (n=186), GI symptoms (n=170), neurological (n=10), Kawasaki signs (n=186), rashes (n=110), conjunctivitis (n=103)	Mechanical ventilation (n=37), IVIG (n=144), systemic steroids (n=91),	Recovered (n=130) ICU admission (n=148) Death (n=4)
George, S 2020	Brunei-Dar	LMIC	12	National surveillance	6.1	7	Travel history (n=0) Contact history (n=12) Comorbidities (n=4)	Fever (n=6), cough (n=6), asymptomatic (n=4)	Antibiotics (n=1)	Recovered (n=12) ICU admission (n=0)
Gonzalez -Cortes, R 2020	Spain	HIC	50	Patients admitted to intensive care units	6.7	31	Travel history (NR) Contact history (NR) Comorbidities (NR)	Dyspnea (n=20), neurological (n=1), Kawasaki (n=27), rashes (n=27)	Mechanical ventilation (n=14), antiviral (n=26), antibiotics (n=43), IVIG (n=15), systemic steroids (n=32), antimalarial (n=29)	Recovered (n=50) ICU admission (n=14)
Kainth, MK 2020	USA	HIC	65	Patients admitted in hospital	9.6	33	Travel history (NR) Contact history (n=33) Comorbidities (n=30)	Fever (n=57), cough (n=32), fatigue (n=26), dyspnea (n=34), GI symptoms (n=40), nasal symptoms or sore throat	Mechanical ventilation (n=5), antiviral (n=4), antibiotics (n=13), systemic steroids	Recovered (n=57) ICU admission (n=22) Death (n=1)

								(n=22), neurological (n=21), rashes (n=5)	(n=7), antimalarial (n=13), inotropes (n=8)	
Kaushik, S 2020	USA	HIC	33	Patients admitted in hospital	9.8	20	Travel history (NR) Contact history (n=13) Comorbidities (n=16)	Fever (n=31), dyspnea (n=11), diarrhea (n=16), nausea or vomiting (n=23), abdominal pain (n=21), neurological (n=4), Kawasaki signs (n=33), rashes (n=7), conjunctivitis (n=12)	Mechanical ventilation (n=5), antiviral (n=7), antibiotics (n=32), systemic steroids (n=17), IVIG (n=18), inotropes (n=17)	Recovered (n=32) ICU admission (n=33) Death (n=1)
Kest, H 2020	USA	HIC	3	Patients admitted in hospital	8.3	1	Travel history (n=0) Contact history (n=1) Comorbidities (n=0)	Fever (n=3), fatigue (n=1), GI symptoms (n=3), neurological (n=2), Kawasaki signs (n=3), rashes (n=3), conjunctivitis (n=3)	Mechanical ventilation (n=2), antibiotics (n=2), IVIG (n=2), systemic steroids (n=3), antimalarial (n=1), inotropes (n=3)	Recovered (n=3) ICU admission (n=3)
Korkmaz, MF 2020	Turkey	LMIC	81	Patients admitted in hospital	9.2	48	Travel history (NR) Contact history (n=75) Comorbidities (n=4)	Fever (n=47), cough (n=42), fatigue (n=15), dyspnea (n=2), GI symptoms (n=3), nasal symptoms or sore throat (n=7), neurological (n=11), asymptomatic (n=17)	Antibiotics (n=42), systemic steroids (n=3)	Recovered (n=81) ICU admission (n=2)
Meslin, P 2020	France	HIC	6	Patients admitted in hospital	0.1	3	Travel history (NR) Contact history (n=4) Comorbidities (n=2)	Fever (n=6), cough (n=1), fatigue (n=1), nausea or vomiting (n=1), nasal symptoms (n=2)	NR	Recovered (n=6) ICU admission (n=0)
Moraleda, C 2020	Spain	HIC	31	Patients admitted in hospital	7.8	18	Travel history (NR) Contact history (n=16)	Fever (n=30), cough (n=11), fatigue (n=5), dyspnea (n=8), GI symptoms (n=27), sore throat or nasal symptoms (n=8),	Mechanical ventilation (n=6), antiviral (n=9), antibiotics (n=28), systemic steroids (n=21), IVIG (n=20)	Recovered (n=29) ICU admission (n=20) Death (n=1)

							Comorbidities (n=10)	neurological (n=10), Kawasaki signs (n=13), rashes (n=23)		
Foong, Ng 2020	UK	HIC	3	Patients admitted in hospital	15.3	2	Travel history (n=0) Contact history (n=0) Comorbidities (n=1)	GI symptoms (n=3), Kawasaki signs (n=3), rashes (n=3), conjunctivitis (n=3)	Antibiotics (n=3), systemic steroids (n=1), IVIG (n=1), inotropes (n=2)	Recovered (n=3) ICU admission (n=3)
Pacquette, D 2020	Canada	HIC	938	National surveillance	NR	463	Travel history (n=106) Contact history (n=305) Comorbidities (NR)	NR	NR	NR
Parri, N 2020	Italy	HIC	130	Data collected through large collaborative networks	5.8	73	Travel history (n=0) Contact history (n=70) Comorbidities (N=34)	Fever (n=67), cough (n=54), dyspnea (n=17), diarrhea (n=10), sore throat or nasal symptoms (n=25), nausea or vomiting (n=15), neurological (n=3), asymptomatic (n=17)	Mechanical ventilation (n=2)	Recovered (n=130) ICU admission (n=9)
Perez, A 2020	USA	HIC	2	Patients admitted in hospital	16.5	1	Travel history (n=0) Contact history (n=0) Comorbidities (N=0)	Fever (n=1), fatigue (n=1), diarrhea (n=1), nausea or vomiting (n=1), abdominal pain (n=1)	NR	Recovered (n=2) ICU admission (n=0)
Sarangi, B 2020	India	LMIC	50	Patients presenting to in hospital	NR	28	Travel history (n=1) Contact history (n=45) Comorbidities (N=2)	Fever (n=17), cough (n=8), fatigue (n=4), diarrhea (n=2), sore throat or nasal symptoms (n=7), neurological (n=2), rashes (n=1),	NR	Recovered (n=50) ICU admission (n=0)

								asymptomatic (n=29), conjunctivitis (n=1)		
Sadiq, M 2020	Pakistan	LMIC	8	Patients admitted in hospital	9.5	7	Travel history (n=0) Contact history (n=8) Comorbidities (N=0)	Fever (n=8), fatigue (n=6), GI symptoms (n=6), neurological (n=3), Kawasaki signs (n=8), rashes (n=5), conjunctivitis (n=7)	Mechanical ventilation (n=1), systemic steroids (n=3), IVIG (n=6),	Recovered (n=5) ICU admission (n=2) Death (n=1)
Swann, OV 2020	UK	HIC	651	Patients admitted in hospitals	5.8	367	Travel history (NR) Contact history (NR) Comorbidities (n=276)	Fever (n=429), cough (n=231), fatigue (n=141), dyspnea (n=172), diarrhea (n=98), nausea or vomiting (n=179), abdominal pain (n=107), sore throat or nasal symptoms (n=132), neurological (n=148), kawasaki signs (n=52), rashes (n=87), conjunctivitis (n=26)	Mechanical ventilation (n=58), antiviral (n=38), antibiotics (n=415), systemic steroids (n=77), inotropes (n=47)	Recovered (n=557) ICU admission (n=116) Death (n=6)
Antunez-Montez, O 2020	5 Latin american Countries	LMIC	409	Patients presenting to hospitals	5.05	222	Travel history (n=0) Contact history (n=232) Comorbidities (N=83)	Fever (n=238), dyspnea (n=102), GI symptoms (n=101), sore throat or nasal symptoms (n=244), neurological (n=48), kawasaki signs (n=95), rashes (n=95), conjunctivitis (n=95), asymptomatic (n=49)	Mechanical ventilation (n=29), antiviral (n=14), IVIG (n=40), systemic steroids (n=63), antimalarial (n=10)	Recovered (n=392) ICU admission (n=52) Death (n=17)
Capone, C 2020	USA	HIC	33	Patients admitted in hospital	8.8	20	Travel history (NR) Contact history (NR) Comorbidities (N=7)	Fever (n=33), cough (n=17), dyspnea (n=17), diarrhea (n=32), nausea or vomiting (n=32), abdominal pain (n=32), neurological (n=19), kawasaki signs (n=21),	Mechanical ventilation (n=6), IVIG (n=33), systemic steroids (n=23), aspirin (n=29)	Recovered (n=33) ICU admission (n=52) Death (n=17)

								rashes (n=21), conjunctivitis (n=21)		
Cura Yayla, B 2020	Turkey	LMIC	220	Patients admitted in hospitals	9.3	106	Travel history (NR) Contact history (n=217) Comorbidities (N=21)	Fever (n=89), cough (n=79), fatigue (n=36), dyspnea (n=9), diarrhea (n=17), nausea or vomiting (n=9), sore throat or nasal symptoms (n=37), neurological (n=20), conjunctivitis (n=3), asymptomatic (n=55)	Mechanical ventilation (n=3), antiviral (n=6), antibiotics (n=40), antimalarial (n=1)	Recovered (n=209) ICU admission (n=3) Death (n=2)
Davies, P 2020	UK	HIC	78	Patients admitted to intensive care units	11.0	52	Travel history (NR) Contact history (NR) Comorbidities (N=17)	Fever (n=78), diarrhea (n=50), nausea or vomiting (n=49), abdominal pain (n=48), kawasaki signs (n=68), rashes (n=35), conjunctivitis (n=23)	Mechanical ventilation (n=36), antiviral (n=1), antibiotics (n=78), systemic steroids (n=57), IVIG (n=59), inotropes (n=65), aspirin (n=45)	Recovered (n=76) ICU admission (n=78) Death (n=2)
de Farias, E 2020	Brazil	LMIC	11	Patients admitted in hospital	5.4	9	Travel history (NR) Contact history (NR) Comorbidities (N=8)	Fever (n=11), kawasaki signs (n=5), rashes (n=5), conjunctivitis (n=5)	Mechanical ventilation (n=7), inotropes (n=7)	Recovered (n=9) ICU admission (n=11) Death (n=2)
Dima, M 2020	Romania	HIC	3	Patients admitted in hospital	Newborns	2	Travel history (n=0) Contact history (n=3) Comorbidities (N=1)	Fever (n=3), cough (n=1), fatigue (n=3), dyspnea (n=3)	antibiotics (n=1), IVIG (n=1), inotropes (n=47)	Recovered (n=3) ICU admission (n=0) Death (n=0)
Han, M 2020	Korea	HIC	91	Patients admitted in 20 hospitals	10.0	53	Travel history (n=15) Contact history (n=72)	Fever (n=27), cough (n=37), fatigue (n=12), dyspnea (n=5), diarrhea (n=11), nausea or vomiting (n=6),	antiviral (n=13), antimalarial (n=2)	Recovered (n=91) ICU admission (n=0) Death (n=0)

							Comorbidities (N=6)	abdominal pain (n=6), sore throat or nasal symptoms (n=8), neurological (n=12), asymptomatic (n=20)		
Ibrahim, L 2020	Australia	HIC	4	Patients presenting to hospital	13.1	1	Travel history (n=3) Contact history (n=4) Comorbidities (N=1)	Fever (n=1), cough (n=2), fatigue (n=4), diarrhea (n=1), sore throat or nasal symptoms (n=2), neurological (n=3)	Only supportive care	Recovered (n=4) ICU admission (n=0) Death (n=0)
Kilani, M 2020	Jordan	LMIC	61	Patients admitted in hospital	6.9		Travel history (n=0) Contact history (NR) Comorbidities (N=2)	Fever (n=11), cough (n=7), fatigue (n=12), diarrhea (n=10), sore throat or nasal symptoms (n=21), neurological (n=12), rashes (n=5), conjunctivitis (n=2), asymptomatic (n=27)	antimalarial (n=6)	Recovered (n=61) ICU admission (n=0) Death (n=0)
Okarska-Napierala, P 2020	Poland	HIC	9	Nationwide survey	10.35	4	Travel history (n=0) Contact history (n=2) Comorbidities (N=2)	Fever (n=9), cough (n=2), fatigue (n=2), dyspnea (n=2), diarrhea (n=5), nausea or vomiting (n=5), abdominal pain (n=5), neurological (n=5), kawasaki signs (n=9), rashes (n=6), conjunctivitis (n=4)	IVIG (n=7), systemic steroids (n=7), aspirin (n=6)	Recovered (n=4) ICU admission (n=1) Death (n=0)
Mahmoudi, S 2020	Iran	LMIC	35	Patients admitted in hospital	7.5	22	Travel history (n=0) Contact history (n=29) Comorbidities (N=18)	Fever (n=27), cough (n=28), fatigue (n=5), dyspnea (n=10), diarrhea (n=9), nausea or vomiting (n=10), abdominal pain (n=4), sore throat or nasal symptoms (n=3), neurological (n=7)	antiviral (n=30), antibiotics (n=35), antimalarial (n=22)	Recovered (n=31) ICU admission (n=7) Death (n=4)

Mamishi, S 2020	Iran	LMIC	45	Patients admitted in 3 hospitals	8.0	24	Travel history (n=0) Contact history (n=14) Comorbidities (N=6)	Fever (n=41), cough (n=16), fatigue (n=11), dyspnea (n=10), diarrhea (n=16), nausea or vomiting (n=23), abdominal pain (n=26), sore throat or nasal symptoms (n=7), kawasaki signs (n=31), rashes (n=24), conjunctivitis (n=23)	IVIg (n=18), systemic steroids (n=27),	Recovered (n=40) ICU admission (n=5) Death (n=5)
Mithal, L 2020	USA	HIC	18	Patients presenting to hospital	0.134	7	Travel history (n=0) Contact history (n=14) Comorbidities (N=0)	Fever (n=14), cough (n=8), fatigue (n=5), dyspnea (n=1), diarrhea (n=4), nausea or vomiting (n=4), sore throat or nasal symptoms (n=5), rashes (n=1), conjunctivitis (n=2), asymptomatic (n=1)	antibiotics (n=6)	Recovered (n=18) ICU admission (n=0) Death (n=0)
Newman, A 2020	USA	HIC	4	Patients admitted in hospital	10.9	4	Travel history (n=0) Contact history (n=0) Comorbidities (N=4)	Fever (n=3), cough (n=4), fatigue (n=2), dyspnea (n=1), nausea or vomiting (n=1), abdominal pain (n=1), sore throat or nasal symptoms (n=1)	Mechanical ventilation (n=1), antiviral (n=1), antibiotics (n=1), antimalarial (n=1)	Recovered (n=4) ICU admission (n=1) Death (n=0)
Torres, J 2020	Chile	HIC	27	Patients admitted in hospital	6.5	14	Travel history (n=0) Contact history (n=9) Comorbidities (N=7)	Fever (n=27), cough (n=7), diarrhea (n=17), nausea or vomiting (n=13), abdominal pain (n=17), kawasaki signs (n=18), rashes (n=14), conjunctivitis (n=13)	Mechanical ventilation (n=12), antibiotics (n=24), IVIg (n=19), systemic steroids (n=17) inotropes (n=12), aspirin (n=17)	Recovered (n=27) ICU admission (n=16) Death (n=0)
Saha, S 2020	Bangladesh	LMIC	26		0.02	16	Travel history (n=0)	Fever (n=14)		Recovered (n=12)

				Patients admitted in hospital			Contact history (n=8) Comorbidities (N=17)		Mechanical ventilation (n=25)	ICU admission (n=0) Death (n=4)
Gale, C 2020	UK	HIC	66	Population based surveillance study	Newborns	27	Travel history (n=0) Contact history (n=34) Comorbidities (N=18)	Fever (n=35), cough (n=11), fatigue (n=33), dyspnea (n=24), diarrhea (n=4), nausea or vomiting (n=33), sore throat or nasal symptoms (n=26), neurological (n=5), rashes (n=2), asymptomatic (n=7)	Mechanical ventilation (n=3), antiviral (n=2), antibiotics (n=46), IVIG (n=1), systemic steroids (n=2), inotropes (n=1)	Recovered (n=58) ICU admission (n=4) Death (n=1)
Schwartz, D 2020	Iran	LMIC	17	Patients admitted in hospital	Newborns	10	Travel history (n=0) Contact history (n=11) Comorbidities (NR)	Fever (n=4), cough (n=3), fatigue (n=17), dyspnea (n=12), diarrhea (n=1), abdominal pain (n=1), asymptomatic (n=2)	Mechanical ventilation (n=4), antibiotics (n=5), antimalarial (n=1), inotropes (n=1)	Recovered (n=7) ICU admission (n=4) Death (n=2)
Schwartz, S 2020	USA	HIC	4	Patients admitted in hospital	12.0	2	Travel history (n=0) Contact history (n=0) Comorbidities (N=3)	Fever (n=4), cough (n=3), fatigue (n=3), dyspnea (n=3), diarrhea (n=2), nausea or vomiting (n=3), abdominal pain (n=2), sore throat or nasal symptoms (n=2), rashes (n=1)	Mechanical ventilation (n=2), antiviral (n=2), systemic steroids (n=1), inotropes (n=1)	Recovered (n=4) ICU admission (n=4) Death (n=0)
Jain, S 2020	India	LMIC	23	Patients admitted in hospital	7.3	11	Travel history (n=0) Contact history (n=8) Comorbidities (NR)	Fever (n=23), cough (n=0), fatigue (n=3), dyspnea (n=11), diarrhea (n=15), nausea or vomiting (n=15), abdominal pain (n=12), sore throat or nasal symptoms (n=0), kawasaki signs (n=23),	Mechanical ventilation (n=9), IVIG (n=15), systemic steroids (n=22) inotropes (n=15)	Recovered (n=22) ICU admission (n=15) Death (n=1)

								rashes (n=14), conjunctivitis (n=11)		
Webb, K 2020	South Africa	LMIC	23	Patients admitted in hospital	6.6	6	Travel history (n=0) Contact history (n=3) Comorbidities (N=8)	Fever (n=23), cough (n=0), fatigue (n=8), dyspnea (n=10), diarrhea (n=13), nausea or vomiting (n=0), abdominal pain (n=15), sore throat or nasal symptoms (n=0), neurological (n=5), kawasaki signs (n=16), rashes (n=20), conjunctivitis (n=15)	Mechanical ventilation (n=6), IVIG (n=23), systemic steroids (n=15) inotropes (n=9), aspirin (n=17)	Recovered (n=15) ICU admission (n=12) Death (n=0)
van der Zalm, M 2020	South Africa	LMIC	159	Patients presenting to hospital	4.5	88	Travel history (NR) Contact history (NR) Comorbidities (N=33)	Fever (n=50), cough (n=72), fatigue (n=0), dyspnea (n=27), diarrhea (n=22), nausea or vomiting (n=18), abdominal pain (n=0), sore throat or nasal symptoms (n=18), neurological (n=20), kawasaki signs (n=3), rashes (n=6)	Mechanical ventilation (n=4)	Recovered (n=149) ICU admission (n=11) Death (n=1)
Sethuraman, U 2020	USA	HIC	34	Patients presenting to emergency department of the hospital	6.0	16	Travel history (n=0) Contact history (n=6) Comorbidities (N=11)	Fever (n=30), cough (n=0), fatigue (n=0), dyspnea (n=1), diarrhea (n=13), nausea or vomiting (n=14), abdominal pain (n=20), sore throat or nasal symptoms (n=9), rashes (n=19), conjunctivitis (n=9)	Mechanical ventilation (n=8), IVIG (n=24), inotropes (n=10), aspirin (n=24)	Recovered (n=34) ICU admission (n=24) Death (n=0)
Onal, P 2020	Turkey		37		10.0	20	Travel history (n=0)	Fever (n=26), cough (n=28), fatigue (n=18), dyspnea (n=13), diarrhea	Mechanical ventilation (n=1), antivirals (n=22)	Recovered (n=37)

		LMIC		Patients presenting to hospital			Contact history (n=29) Comorbidities (N=10)	(n=4), nausea or vomiting (n=8), abdominal pain (n=12), sore throat or nasal symptoms (n=12), neurological (n=11), asymptomatic (n=2)	antibiotics (n=24), IVIG (n=19), antimalarials (n=14)	ICU admission (n=10) Death (n=0)
Rabha, A 2020	Brazil	LMIC	115	Patients admitted in hospital	3.3	66	Travel history (n=0) Contact history (n=86) Comorbidities (N=30)	Fever (n=79), cough (n=59), fatigue (n=31), dyspnea (n=15), diarrhea (n=15), nausea or vomiting (n=20), abdominal pain (n=10), sore throat or nasal symptoms (n=17), rashes (n=5), neurological (n=23), asymptomatic (n=3)	antibiotics (n=24)	Recovered (n=115) ICU admission (n=12) Death (n=0)
Shahbaz nejad, L 2020	Iran	LMIC	10	Patients admitted in hospital	5.4	6	Travel history (n=0) Contact history (n=10) Comorbidities (N=0)	Fever (n=10), fatigue (n=2), dyspnea (n=2), diarrhea (n=7), nausea or vomiting (n=6), abdominal pain (n=9), sore throat or nasal symptoms (n=4), rashes (n=8), kawasaki signs (n=10), neurological (n=1), conjunctivitis (n=3)	Antivirals (n=1), antibiotics (n=10), IVIG (n=6), systemic steroids (n=2), antimalarial (n=8) inotropes (n=2), aspirin (n=3)	Recovered (n=9) ICU admission (n=3) Death (n=1)
Storch-de-Garcia, P 2020	Spain	HIC	39	Patients admitted in hospital	8.5	23	Travel history (n=0) Contact history (n=27) Comorbidities (N=5)	Fever (n=32), cough (n=20), fatigue (n=13), dyspnea (n=9), diarrhea (n=14), nausea or vomiting (n=15), abdominal pain (n=12), sore throat or nasal symptoms (n=18), rashes (n=10), kawasaki signs	Antivirals (n=13), antibiotics (n=25), IVIG (n=4), systemic steroids (n=15), antimalarial (n=15), aspirin (n=12)	Recovered (n=39) ICU admission (n=14) Death (n=0)

								(n=11), neurological (n=7), asymptomatic (n=7)		
García-Salido, A 2020	Spain	HIC	74	47 pediatric intensive care centres	7.7	46	Travel history (n=0) Contact history (n=13) Comorbidities (N=22)	Fever (n=61), cough (n=26), fatigue (n=48), dyspnea (n=23), diarrhea (n=33), nausea or vomiting (n=38), abdominal pain (n=33), sore throat or nasal symptoms (n=11), kawasaki signs (n=45), neurological (n=22)	Mechanical ventilation (n=18), antivirals (n=35), antibiotics (n=65), IVIG (n=25), systemic steroids (n=49), antimalarial (n=43), inotropes (n=37)	Recovered (n=65) ICU admission (n=74) Death (n=3)
Lima-setta, F 2020	Brazil	LMIC	56	17 pediatric intensive care centres	6.3	39	Travel history (n=0) Contact history (n=27) Comorbidities (N=11)	Fever (n=56), cough (n=16), fatigue (n=28), dyspnea (n=9), diarrhea (n=30), nausea or vomiting (n=21), abdominal pain (n=30), sore throat or nasal symptoms (n=17), rashes (n=38), kawasaki signs (n=26), neurological (n=27), conjunctivitis (n=26)	Mechanical ventilation (n=6), antivirals (n=5), antibiotics (n=33), IVIG (n=50), systemic steroids (n=31), aspirin (n=25)	Recovered (n=53) ICU admission (n=56) Death (n=1)
Zachariah, P 2020	USA	HIC	50	Patients admitted in hospital	11.5	27	Travel history (n=0) Contact history (n=9) Comorbidities (N=33)	Fever (n=40), cough (n=23), dyspnea (n=17), diarrhea (n=7), nausea or vomiting (n=7), abdominal pain (n=7), sore throat or nasal symptoms (n=6), neurological (n=3)	Mechanical ventilation (n=9), antivirals (n=4), IVIG (n=1), antimalarial (n=15)	Recovered (n=47) ICU admission (n=9) Death (n=1)
Kalamdani, P 2020	India	LMIC	12	Patients admitted in hospital	Newborns	8	Travel history (n=0) Contact history (n=12)	Fever (n=3), fatigue (n=2)	NR	Recovered (n=12) ICU admission (n=0) Death (n=0)

							Comorbidities (NR)			
Colomer, B 2020	Spain	HIC	40	Cases from a National Registry supported by the Spanish Society of Neonatology	Newborns	25	Travel history (n=0) Contact history (n=36) Comorbidities (N=15)	Fever (n=18), cough (n=9), fatigue (n=4), dyspnea (n=7), diarrhea (n=2), nausea or vomiting (n=4), sore throat or nasal symptoms (n=5), rashes (n=1), asymptomatic (n=10)	Antivirals (n=1), antibiotics (n=8), IVIG (n=19), antimalarial (n=5)	Recovered (n=40) ICU admission (n=8) Death (n=0)
Dhanalakshmi, K 2020	India	LMIC	19	Patients admitted in hospital	7.2	8	Travel history (n=0) Contact history (n=0) Comorbidities (N=1)	Fever (n=19), dyspnea (n=8), diarrhea (n=3), nausea or vomiting (n=6), abdominal pain (n=8), sore throat or nasal symptoms (n=9), rashes (n=12), neurological (n=6), kawasaki signs (n=7), conjunctivitis (n=9)	Antibiotics (n=19), IVIG (n=15), systemic steroids (n=11) inotropes (n=6), aspirin (n=16)	Recovered (n=19) ICU admission (n=12) Death (n=0)
Falah, N 2020	Pakistan	LMIC	10	Patients admitted in 2 hospitals	6.0	8	Travel history (n=0) Contact history (n=2) Comorbidities (N=0)	Fever (n=10), cough (n=2), fatigue (n=4), dyspnea (n=2), diarrhea (n=3), abdominal pain (n=5), sore throat or nasal symptoms (n=6), rashes (n=8), neurological (n=6), kawasaki signs (n=5), conjunctivitis (n=9)	Antivirals (n=1), antibiotics (n=6), IVIG (n=9), systemic steroids (n=3) inotropes (n=4), aspirin (n=7)	Recovered (n=10) ICU admission (n=7) Death (n=0)
Zheng, G 2020	China	LMIC	52	Patients admitted in 11 hospitals	8.5	28	Travel history (n=52) Contact history (n=42) Comorbidities (N=0)	Fever (n=21), cough (n=25), fatigue (n=5), diarrhea (n=1), nausea or vomiting (n=1), abdominal pain (n=1), sore throat or nasal	Antivirals (n=43), antibiotics (n=25)	Recovered (n=52) ICU admission (n=0) Death (n=0)

								symptoms (n=3), asymptomatic (n=13)		
Almoosa, Z 2020	Saudi Arabia	HIC	10	Patients admitted in 2 hospitals	7.6	5	Travel history (n=0) Contact history (n=6) Comorbidities (N=5)	Fever (n=10), fatigue (n=5), dyspnea (n=3), diarrhea (n=7), nausea or vomiting (n=9), abdominal pain (n=9), Kawasaki signs (n=10), rashes (n=10), conjunctivitis (n=9)	Mechanical ventilation (n=2), antivirals (n=7), antibiotics (n=10), IVIG (n=10), antimalarials (n=10), systemic steroids (n=17) inotropes (n=5), aspirin (n=4)	Recovered (n=8) ICU admission (n=8) Death (n=2)
Alsharrah, D 2020	Kuwait	HIC	134	Patients admitted in hospital	8.7	74	Travel history (n=19) Contact history (n=110) Comorbidities (N=15)	Fever (n=75), cough (n=100), asymptomatic (n=91)	Antibiotics (n=11)	Recovered (n=133) ICU admission (n=0) Death (n=0)
Prata-Barbosa, A 2020	Brazil	LMIC	79	19 pediatric intensive care centres	4.8	43	Travel history (NR) Contact history (NR) Comorbidities (N=32)	Fever (n=59), cough (n=40), fatigue (n=35), dyspnea (n=23), diarrhea (n=16), nausea or vomiting (n=16), abdominal pain (n=16), sore throat or nasal symptoms (n=17), kawasaki signs (n=5)	Mechanical ventilation (n=14), antivirals (n=34), antibiotics (n=60), systemic steroids (n=18) inotropes (n=12), aspirin (n=17)	Recovered (n=71) ICU admission (n=79) Death (n=2)
Bayesheva, D 2020	Kazakhstan	LMIC	650	Data was reported from the official medical electronic database of the Country	7.1	366	Travel history (NR) Contact history (NR) Comorbidities (N=76)	Fever (n=59), cough (n=96), fatigue (n=7), dyspnea (n=12), diarrhea (n=13), asymptomatic (n=315), sore throat or nasal symptoms (n=119), rashes (n=1)	Mechanical ventilation (n=3)	Recovered (n=650) ICU admission (n=6) Death (n=0)
Bustos-Cordova, E 2020	Mexico		50		5.9	35	Travel history (NR)	Fever (n=35), cough (n=22), fatigue (n=21), dyspnea (n=10), diarrhea		Recovered (n=50)

		LMIC		Patients presenting to tertiary care centre outpatient department			Contact history (NR) Comorbidities (N=26)	(n=11), nausea or vomiting (n=11), abdominal pain (n=11), sore throat or nasal symptoms (n=25), rashes (n=4), kawasaki signs (n=1), conjunctivitis (n=11)	Mechanical ventilation (n=2), antibiotics (n=15)	ICU admission (n=2) Death (n=1)
Bhavsar, M 2020	USA	HIC	81	Patients admitted in 12 hospitals in the city	14.7	40	Travel history (NR) Contact history (NR) Comorbidities (N=21)	Fever (n=63), cough (n=38), diarrhea (n=26), nausea or vomiting (n=26), abdominal pain (n=26), neurological (n=7), rashes (n=8), conjunctivitis (n=7)	Mechanical ventilation (n=3), antivirals (n=6), IVIG (n=1), systemic steroids (n=15), antimalarials (n=10), inotropes (n=9), aspirin (n=1)	Recovered (n=71) ICU admission (n=28) Death (n=1)
Montoya, J 2020	Peru	LMIC	69	Cancer patients admitted to tertiary care centres	6.0	44	Travel history (n=0) Contact history (n=20) Comorbidities (N=69)	Fever (n=12), cough (n=12), dyspnea (n=11), diarrhea (n=3), nausea or vomiting (n=3), abdominal pain (n=2), sore throat or nasal symptoms (n=11), rashes (n=1), asymptomatic (n=37)	Antibiotics (n=9), interferon (n=9), systemic steroids (n=9)	Recovered (n=56) ICU admission (n=3) Death (n=7)

NR= Not reported

LMIC: Low and middle-income Country, HIC: High-income Country

Table 4: Age Distribution from 91 studies of disease prevalence

Age	Frequency (%)
0 to ≤5 years	3149 (36.9)
>5 to ≤10 years	1668 (19.6)
>10 years	3712 (43.5)
Total	8529

Table 5: Age Distribution from 67 case series of clinical features and outcomes

	Age bands		
	0 to ≤5 years	>5 to ≤10 years	>10 years
Clinical features Frequency (%)			
Fever	99/181 (54.7)	87/133 (65.4)	60/132 (45.4)
Asymptomatic	43/1053 (4.0)	45/654 (7.0)	48/880 (5.4)
Cough	46/181 (25.4)	33/133 (24.8)	23/132 (17.4)
Nasal symptoms/sore throat	22/181 (12.1)	16/133 (12.0)	5/132 (3.8)
Dyspnea	15/181 (8.3)	10/133 (7.5)	13/132 (9.9)
Diarrhea	29/181 (16.0)	48/133 (36.1)	36/132 (27.3)
Nausea and vomiting	29/181 (16.0)	40/133 (30.0)	33/132 (25.0)
Abdominal pain	27/181 (15.0)	47/133 (35.3)	30/132 (22.7)
Fatigue	13/181 (7.2)	7/133 (5.2)	5/132 (3.8)
Neurological signs	8/181 (4.4)	21/133 (15.8)	16/132 (12.1)
Kawasaki signs	15/181 (8.3)	24/133 (18.0)	8/132 (6.0)
Rash	24/181 (13.2)	27/133 (20.3)	20/132 (15.1)
Conjunctivitis	23/181 (12.7)	8/133 (6.0)	18/132 (13.6)
Outcomes Frequency (%)			
Recovered	176/196 (89.8)	119/127 (93.7)	146/160 (91.2)
Severe/ICU admission	188/1708 (11.0)	102/834 (12.2)	131/1134 (11.6)
Not yet discharged	19/196 (9.7)	6/127 (4.7)	8/160 (5.0)
Deaths	1/1360 (0.07)	2/742 (0.3)	11/908 (1.2)

Table 6: Clinical symptoms among MISC from 31 studies

Characteristics	Events/total patients	Mean proportion % (95% CI)
Comorbidity	264/1182	24.7 (20.1-29.9)
Fever	1008/1208	94.2 (88.7-97.1)
Kawasaki shock/sign	708/1208	68.0 (56.0-78.1)
Abdominal pain	313/548	58.1 (49.6-66.1)
Diarrhea	308/563	54.0 (45.9-61.9)
Conjunctivitis	461/1163	49.2 (40.2-58.2)
Nausea/vomiting	280/563	48.7 (38.5-59.0)
Rashes	540/1163	46.5 (43.4-49.7)
Dyspnea	220/1181	22.4 (17.1-28.8)
Neurological symptoms	184/1206	19.0 (12.8-27.3)
Fatigue	104/626	16.3 (9.6-26.3)
Cough	94/766	15.1 (10.1-22.2)
Nasal symptoms	310/1124	12.1 (6.9-20.5)
Pharyngeal erythema	298/1099	10.3 (5.5-18.6)
Clinical management		
IVIG	618/1207	69.1 (55.1-80.4)
Inotropes	255/934	45.5 (34.3-57.2)
Antibiotics	317/1021	38.6 (19.9-61.3)
Aspirin	201/951	31.7 (19.5-47.1)
Systemic steroids	522/1207	52.9 (41.6-63.8)
Mechanical ventilation	208/1204	20.2 (13.9-28.4)
Antimalarial	60/954	7.3 (3.0-16.8)
Antiviral	63/1015	6.9 (3.8-12.4)
Clinical outcomes		
Recovered	1099/1208	91.8 (86.8-95.1)
ICU admission	638/1208	47.1 (43.1-51.1)
Deaths	39/1208	4.8 (3.6-6.3)

Table 7: Clinical symptoms among neonates from 11 studies

Characteristics	Events/total patients	Mean proportion % (95% CI)
Comorbidity	53/184	28.0 (16.5-43.3)
Fever	90/184	47.6 (35.8-59.7)
Dyspnea	50/146	39.1 (22.1-59.2)
Inability to feed/Lethargy	62/158	35.4 (16.7-59.9)
Nausea/vomiting	38/146	34.4 (25.9-44.0)
Nasal symptoms	36/146	29.9 (22.3-38.9)
Cough	28/158	19.2 (13.6-26.3)
Asymptomatic	21/146	16.6 (11.2-23.9)
Pharyngeal erythema	8/146	11.4 (4.8-24.9)
Diarrhea	8/146	7.6 (4.1-13.4)
Neurological symptoms	5/146	7.3 (3.8-13.5)
Rashes	3/146	5.3 (2.4-11.0)
Clinical management		
Antibiotics	86/166	48.7 (39.6-58.0)
Mechanical ventilation	8/140	10.7 (5.2-20.8)
Antimalarial	6/140	9.6 (5.1-17.6)
Antiviral	3/140	6.4 (3.0-12.9)
IVIG	2/140	6.3 (2.4-15.4)
Inotropes	2/140	6.3 (2.4-15.4)
Systemic steroids	2/140	6.3 (2.4-15.4)
Clinical outcomes		
Recovered	146/184	77.8 (55.7-90.7)
ICU admission	22/184	16.0 (7.6-30.7)
Deaths	7/184	8.8 (4.9-15.3)

Table 8: Quality assessment of included studies (N=129)

Study and year	Was the study question or objective clearly stated?	Was the study population clearly and fully described, including a case definition?	Were the cases consecutive?	Were the subjects comparable?	Was the intervention clearly described?	Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Was the length of follow-up adequate?	Were the statistical methods well described?	Were the results well described?	Overall Quality (Good, fair or poor)
Qiu, H 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Wang, D 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Zheng, F 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	No	5
Xia, W 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	6
Feng, K 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	6
Cai, J 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	6
Wei, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Su, L 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Zhou, Y 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Sun, D 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Liu, W 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Hu, Z 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Liu, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Liu, H 2020	Yes	No	Yes	Yes	NA	Yes	No	Yes	No	5
Lou, MX 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Zhang, T 2020	Yes	No	No	Yes	NA	Yes	Yes	Yes	Yes	6
Li, Y 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Ji, LN 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Tagarro, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Chen, A 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	No	5
See, KC 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8

Zhang, GX 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Cheng, X 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Tang, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Zhu, L 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Tan, X 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Ma, H 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Shen, Q 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Schwierzeck, V 2020	Yes	No	Yes	Yes	NA	Yes	No	Yes	No	5
Jiang, JY 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Riphagen, S 2020	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	Yes	7
Shekerdemian, LS 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Verdoni, L 2020	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	Yes	7
Rahimzadeh, G 2020	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	Yes	7
Tullie, L 2020	Yes	No	No	Yes	NA	Yes	Yes	Yes	Yes	6
Sajid, MI 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Zhang, ZJ 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Zeng, L 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Salvatori, G 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Zhang, X 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Wu, HP 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Zhang, H 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Chao, JY 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Eghbali, A 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Chiotos, K 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Flores, V 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
García-Salido, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Cabrero-Hernández, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Waltuch, T 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7

Kakuya, F 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Soltani, J 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Toubiana, J 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Foster, CE 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
White, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Lin, EE 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	No	5
Gao, Y 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Harman, K 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Blondiaux, E 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Pouletty, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Whittaker, E 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Cheung, EW 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Lu, X 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
CDC, COVID 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Gotzinger, F 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Dong, Y 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Abdel-Mannan, O 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Guha, A 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Bhumbra, S 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Bisogno, G 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Blumfield, E 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Derespina, KR 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Feldstein, LR 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6

George, S 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Gonzalez-Cortes, R 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Kainth, MK 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Kaushik, S 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Kest, H 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Korkmaz, MF 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Meslin, P 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Moraleda, C 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	6
Foong, Ng 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Pacquette, D 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Parri, N 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Perez, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	No	6
Sarang, B 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	6
Sadiq, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Swann, OV 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Antunez-Montez, O 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Capone, C 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Cura Yayla, B 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	6
Davies, P 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
de Farias, E 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Dima, M 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Han, M 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Ibrahim, L 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Kilani, M 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Okarska-Napierala, P 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	6

Mahmoudi, S 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Mamishi, S 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Mithal, L 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Newman, A 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Torres, J 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Saha, S 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	No	5
Gale, C 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	6
Schwartz, D 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	No	5
Schwartz, S 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Jain, S 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Webb, K 2020	Yes	No	No	Yes	NA	Yes	No	Yes	Yes	5
van der Zalm, M 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	No	6
Sethuraman, U 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Onal, P 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Rabha, A 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8
Shahbaznejad, L 2020	Yes	No	No	Yes	NA	Yes	Yes	Yes	Yes	6
Storch-de-Garcia, P 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
García-Salido, A 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Lima-setta, F 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Zachariah, P 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Kalamdani, P 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Colomer, B 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	8

Dhanalakhmsi, K 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Falah, N 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Zheng, G 2020	Yes	No	Yes	Yes	NA	Yes	Yes	Yes	Yes	7
Almoosa, Z 2020	Yes	Yes	No	Yes	NA	Yes	Yes	Yes	Yes	7
Alsharrah, D 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Prata-Barbosa, A 2020	Yes	Yes	Yes	Yes	NA	Yes	No	Yes	Yes	7
Bayesheva, D 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Bustos-Cordova, E 2020	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	No	7
Bhavsar, M 2020	Yes	Yes	No	Yes	NA	Yes	No	Yes	Yes	6
Montoya, J 2020	Yes	No	Yes	Yes	NA	Yes	No	Yes	Yes	6

Figure1: Flow diagram of the systematic review process

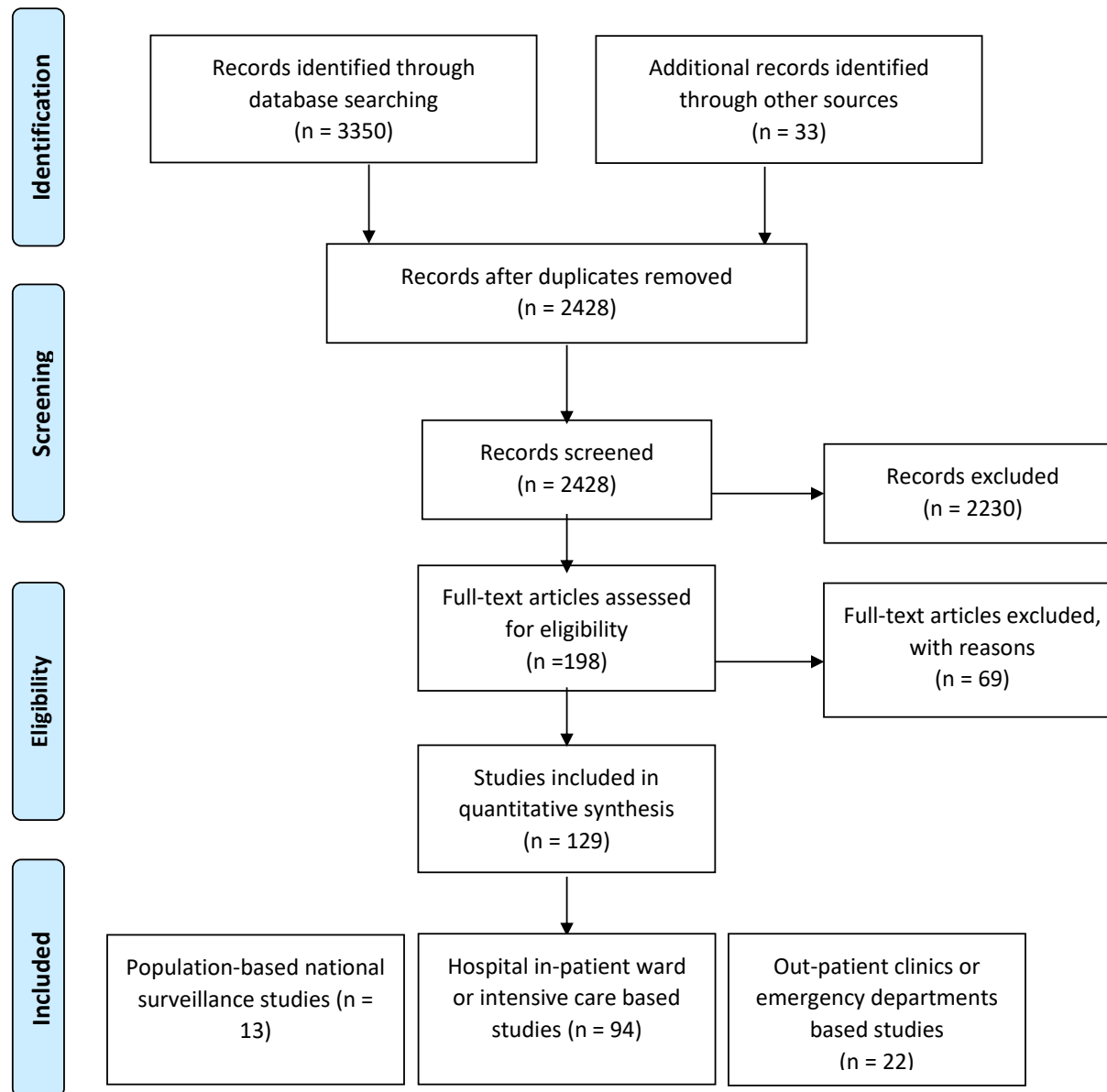


Figure 2: Global map of distribution of the studies included (N=129) in the review



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