

The Prevalence of Clinical Symptoms in Children and Adolescents with Covid-19: A Systematic Review and Meta-Analysis Study

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Abstract

Background

In 2019, an unknown disease called coronavirus disease 2019 (COVID-19) began to spread in China. The disease is now widespread in almost all countries and has endangered the lives of many people. For this reason, a systematic review and meta-analysis were conducted with the aim of assessing the clinical characteristics of the disease in children and adolescents with COVID-19.

Materials and Methods: This systematic review and meta-analysis have been conducted by reviewing most of the epidemiologic studies on the worldwide prevalence of COVID-19 in children and adolescents. The following international databases were used: EMBASE, Scopus, Web of Science, PubMed/Medline, Science Direct, and the Google Scholar Search Engine. The keywords used for searching included "child", "pediatric", "adolescents", "COVID-19", "Coronavirus", and "diagnosis". The data were analyzed using STATA statistic software version 11.0.

Results: The total number of patients was 2579, of which 1467 (56.9%) were male and 1110 (43.1) were female. All patients were in their childhood and adolescence years. At the beginning of the research, 1356 studies were reviewed, of which 987 entered the next reviewing stage. Finally, 14 studies were selected for the systematic review and meta-analysis. The prevalence of fever in children and adolescents was 55.0% (95% CI 0.55 [0.40, 0.70]), of cough 41.0% (95% CI 0.41 [0.27, 0.56]), of nasal discharge 9.0% (95% CI 0.09 [0.05, 0.12]), and of diarrhea 5.0% (95% CI 0.05 [0.02, 0.08]).

Conclusion

The results of this study can be a guide for pediatricians and specialists in the field of infectious diseases to identify the clinical signs of COVID-19 in children and adolescents.

Key Words: Adolescents, Children, Clinical Findings, COVID-19, Diagnostic Findings.

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1- INTRODUCTION

Maintaining and promoting health is one of the most serious global concerns. The importance of health is doubled in childhood and adolescence (1, 2) as these age groups are affected by many types of diseases (3). Infectious diseases are among these types (4), of which COVID-19 is the newest (5, 6). In 2019, an unknown virus began to spread in China. This virus was later called Corona and the disease COVID-19 (7, 8). COVID-19 is now considered a global health emergency and is widespread in all countries and has endangered the lives of many (9, 10). The disease and its symptoms remain largely unknown; therefore, no definite cure has been developed so far. Some of its common symptoms include fever, cough, a runny nose, nausea, vomiting, diarrhea, pain, and fatigue (11-13). Although these symptoms have been reported in patients, no systematic review and meta-analysis study has been conducted so far on the prevalence of the clinical symptoms of COVID-19 in children and adolescents. The present study is conducted to assess these symptoms in children and adolescents with COVID-19 using a systematic review and meta-analysis approach.

2- MATERIALS AND METHODS

2-1. Study protocol

This paper is based on the PARISMA Checklist (14) for Systematic Review and Meta-Analysis studies. The research was carried out by two researchers (MS, HT), and approved by a third researcher (AT) in case of disagreement.

2-2. Search strategy

All epidemiologic studies on the prevalence of COVID-19 worldwide in children and adolescents from 2019 until March 22, 2020 were reviewed. International databases of EMBASE,

Scopus, Web of Science, PubMed/Medline, Science Direct and Google Scholar Search Engine were used.

The keywords used in search included: "child" [MeSH], "pediatric" [MeSH], "adolescents" [MeSH], "COVID-19" [MeSH], "Coronavirus" [MeSH], and "diagnosis" [MeSH]. References of the searched articles were also reviewed to ensure literature saturation on the topic. Article reference were also reviewed.

2-3. Inclusion and Exclusion criteria

All of the articles on the diagnosis COVID-19 in children and adolescents that were published in English were included. Case reports, meta-analyses and articles containing incomplete information were excluded. PICO in this study stands for: **P**: children and adolescents with COVID-19 (patients); **I**: assessment of clinical characteristics; **C**: no disease detected; and **O**: no symptoms (including sputum, fatigue, sore throat, vomiting, tachypnea, diarrhea, nasal discharge, cough, and fever).

2-4. Data extraction

To extract data, a researcher made form was collected from included articles' names, year of publication, age range, country, numbers, gender (male and female), journal name, article references, reported symptoms (sputum, fatigue, sore throat, vomiting, tachypnea, diarrhea, nasal discharge, cough, and fever) or absence of symptoms.

2-5. Study selection

Articles were imported into the Endnote software and duplicate articles were deleted. The data were then extracted by two authors, both fluent in systematic review and meta-analysis. In the event of disagreement between the two authors, the articles was reviewed by a third author.

2-6. Statistical analysis

The normal distribution model was used to analyze the data. The weight of each study had an inverse relationship with its variance. The heterogeneity of the studies was checked using the Q test and I2 index. Due to the considerable heterogeneity among the studies, a random-effects model was utilized for meta-analysis. Meta-regression was used to explore the reasons for heterogeneity. The statistical analyses were performed in STATA software, version 11.0 (College Station, TX, USA)

3- RESULTS

The total number of patients was 2579, of which 1467 were male (56.9%), and 1110 were female (43.1%). All patients

were in their childhood and adolescence years.

3-1. Search results

At the beginning of the research, 1356 studies were searched, of which 987 studies entered the next stage. After reviewing the abstract and the title of the remaining articles, this number was reduced to 231. 181 articles were later removed by re-examination. In the next stage, the complete file of articles was reviewed and 23 more articles were removed from the study. Finally, 14 articles were selected for the systematic review and meta-analysis (**Figure.1**).

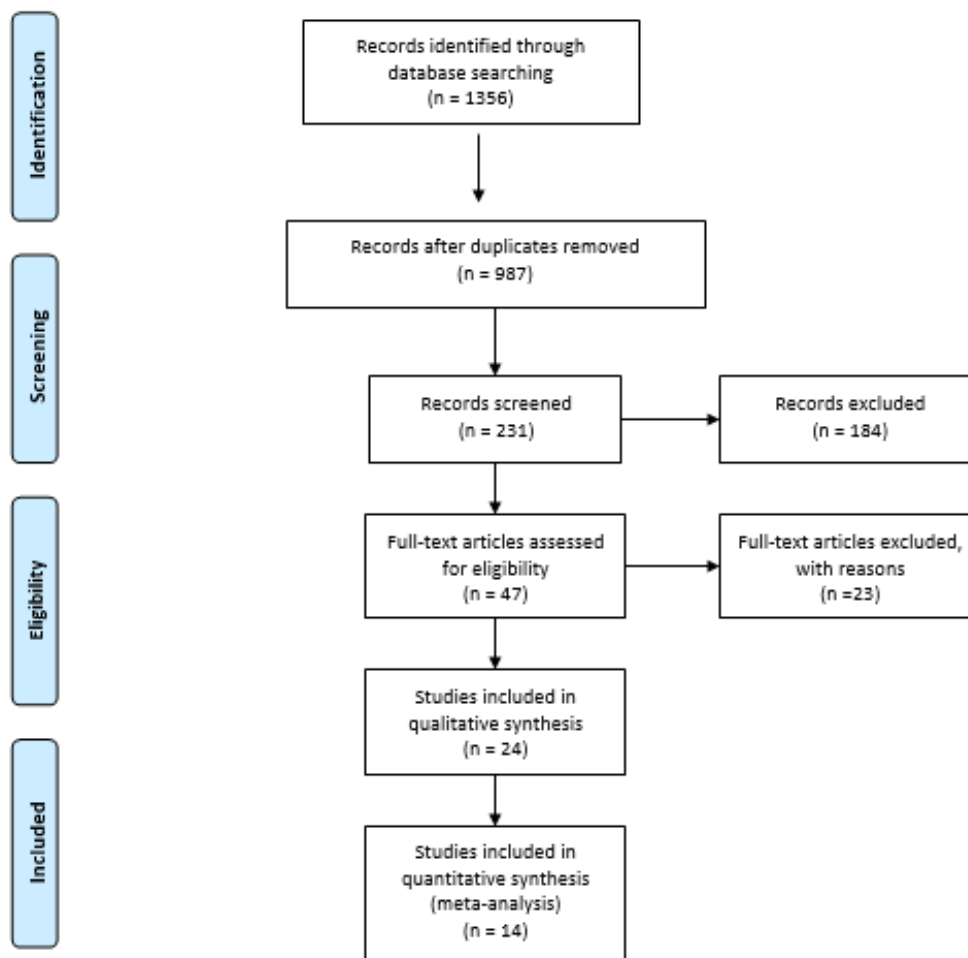


Fig.1: PRISMA flowchart of present study

3-2. Meta-analysis

The prevalence of fever in children and adolescents was 55.0% (95% CI 0.55 [0.40, 0.70]), of cough 41.0% (95% CI 0.41 [0.27, 0.56]), of nasal discharge 9.0% (95% CI 0.09 [0.05, 0.12]), of diarrhea 5.0% (95% CI 0.05 [0.02, 0.08]) , of sore

throat 5.0% (95% CI 0.05 [0.01, 0.10]), of fatigue 6.0% (95% CI 0.06 [0.04, 0.09]), of tachypnea 34.0% (95% CI 0.34 [0.01, 0.67]), of vomiting 10.0% (95% CI 0.10 [0.00, 0.20]), and 13.0% (95% CI 0.13 [0.05, 0.20]) had no symptoms (**Figures 2-10**).

According to **Figure.2**, the prevalence of fever in children and adolescents with COVID-19 is 55.0% (95% CI 0.55 [0.40, 0.70]).

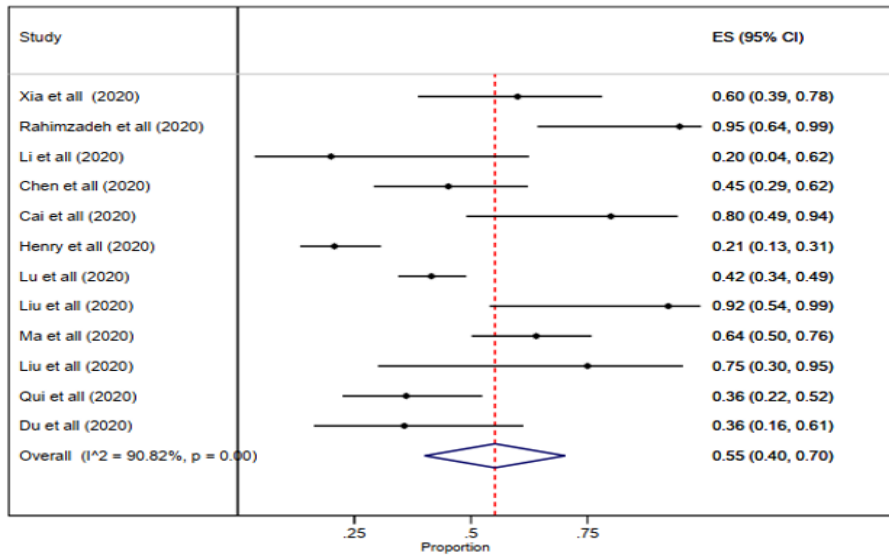


Fig. 2: Prevalence of fever in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.3**, the prevalence of cough in children and adolescents with COVID-19 is 41.0% (95% CI 0.41 [0.27, 0.56]).

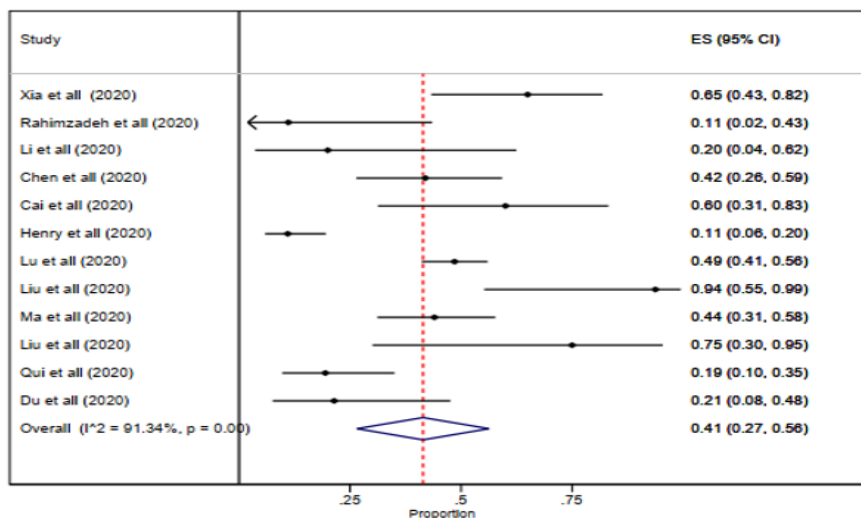


Fig. 3: Prevalence of Cough in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.4**, the prevalence of nasal discharge in children and adolescents with COVID-19 is 9.0% (95% CI 0.09 [0.05, 0.12]).

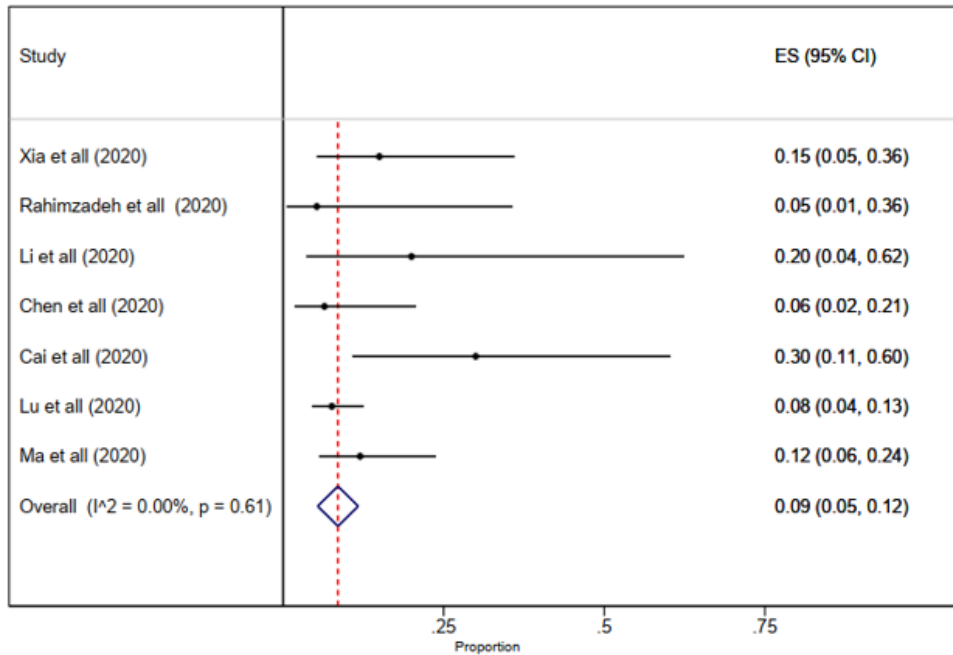


Fig. 4: Prevalence of forest nasal discharge in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.5**, the prevalence of diarrhea in children and adolescents with COVID-19 is 5.0% (95% CI 0.05 [0.02, 0.08]).

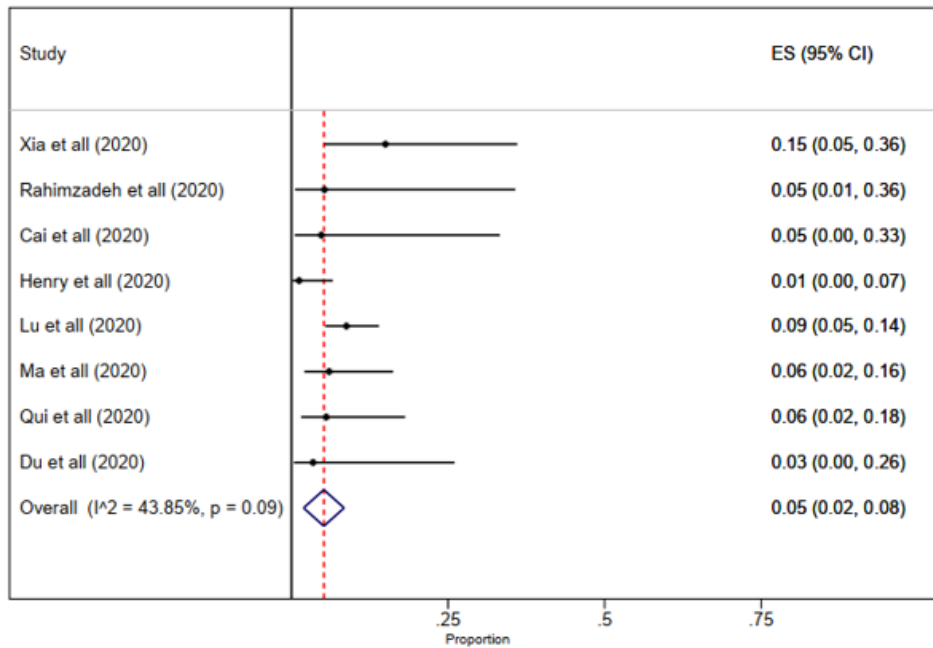


Fig. 5: Prevalence of diarrhea in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.6**, the prevalence of sore throat in children and adolescents with COVID-19 is 5.0% (95% CI 0.05 [0.01, 0.10]).

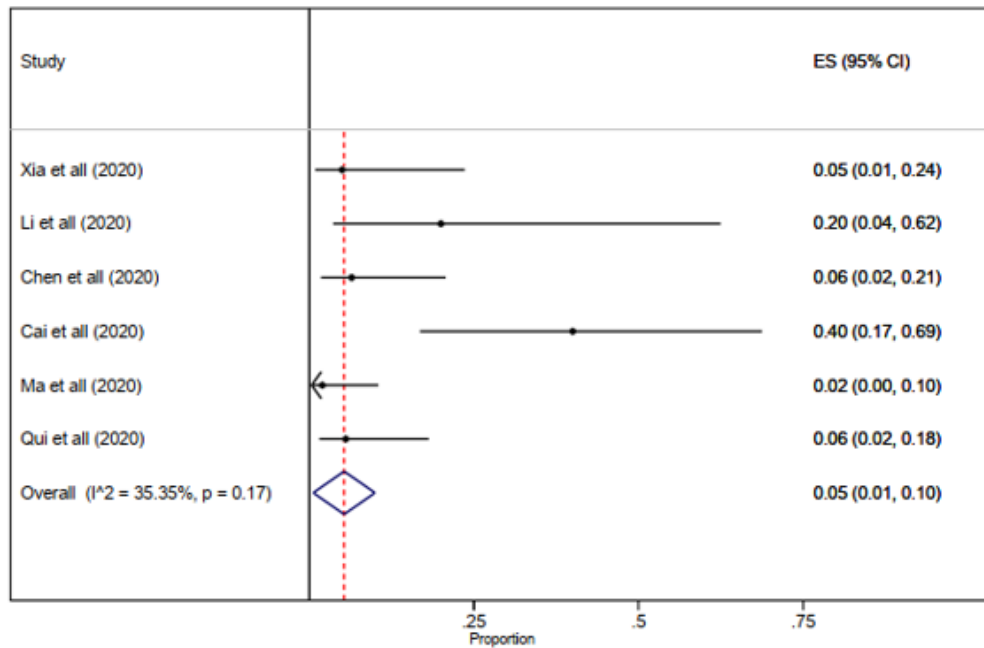


Fig. 6:Prevalence of sore throat in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.7**, the prevalence of fatigue in children and adolescents with COVID-19 is 6.0% (95% CI 0.06 [0.04, 0.09]).

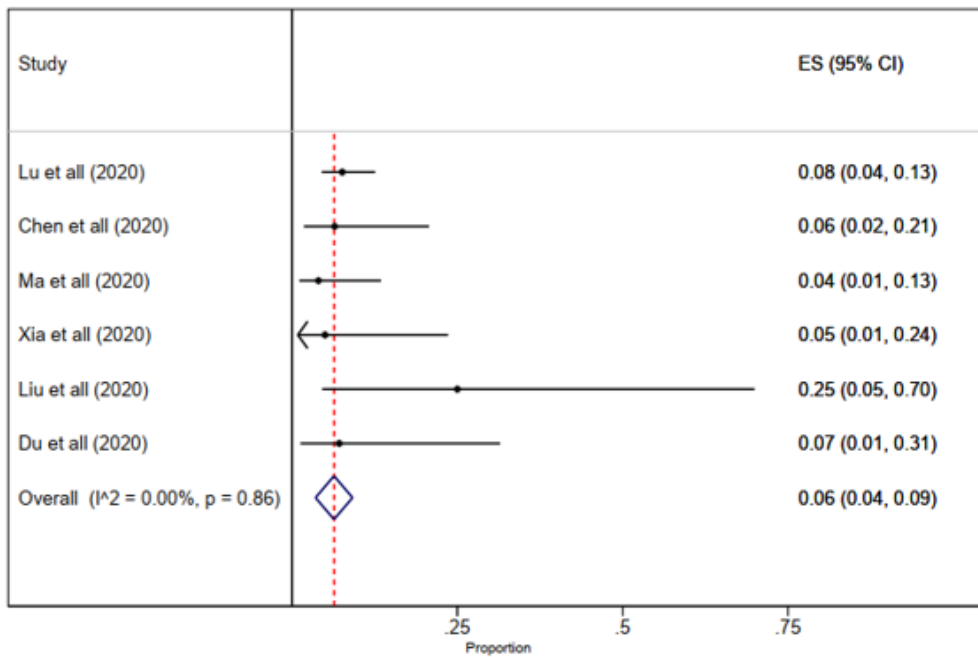


Fig.7: Prevalence of fatigue in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.8**, the prevalence of tachypnea in children and adolescents with COVID-19 is 34.0% (95% CI 0.34 [0.01, 0.67]).

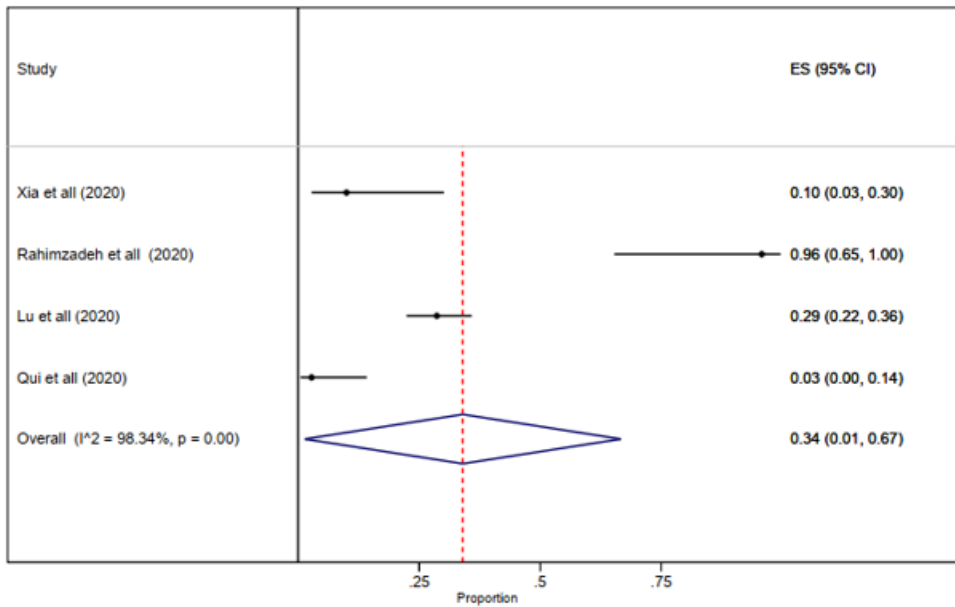


Fig. 8: Prevalence of tachypnea in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.9**, the prevalence of vomiting in children and adolescents with COVID-19 is 10.0% (95% CI 0.10 [0.00, 0.20]).

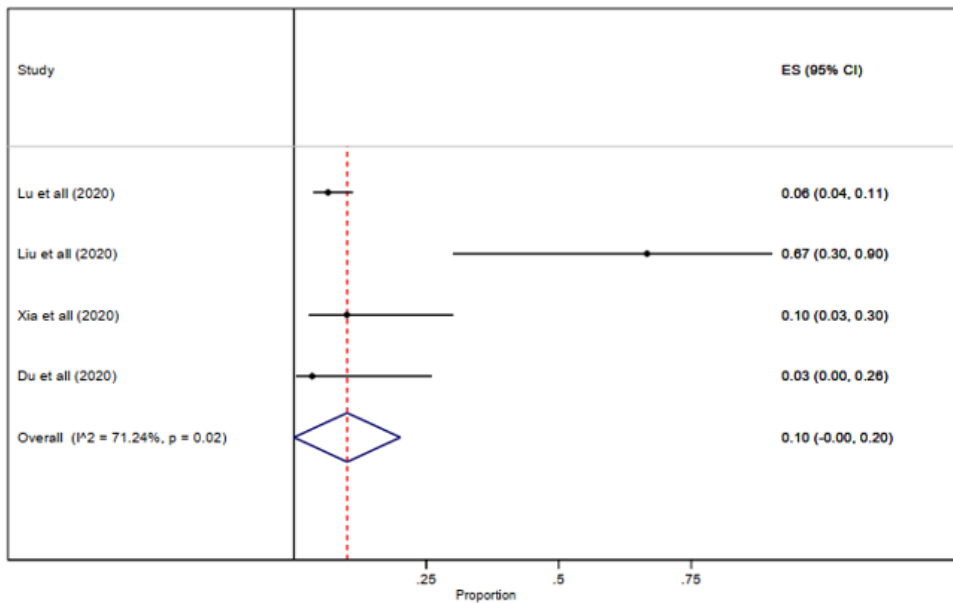


Fig. 9: Prevalence of vomiting in studies entered into the Systematic Review and Meta-Analysis.

According to **Figure.10**, the prevalence of asymptomatic cases among children and adolescents with COVID-19 is 13.0% (95% CI 0.13 [0.05, 0.20]).

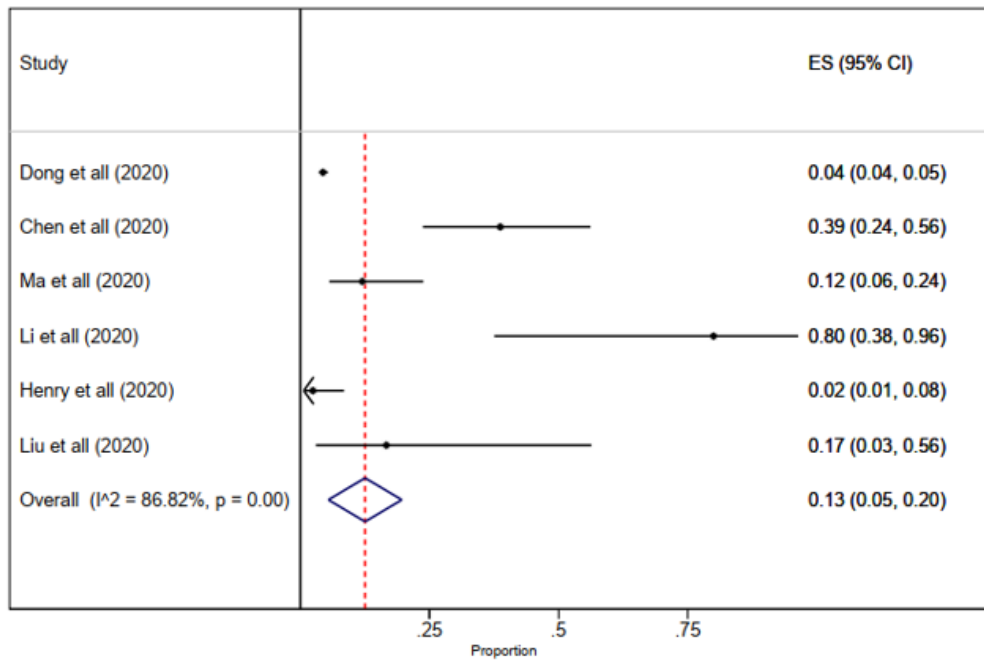


Fig. 10: Prevalence of No symptom in studies entered into the Systematic Review and Meta-Analysis.

4- DISCUSSION

Diagnosis of COVID-19 is a challenge. The aim of this study was to investigate the clinical symptoms in children and adolescents with COVID-19 by a systematic review and meta-analysis. The prevalence of fever in the present study was 55.0% (95% CI 0.55 [0.40, 0.70]). The study of Ma et al. showed that fever is one of the most important symptoms in patients infected with the coronavirus (24). In the systematic review and meta-analysis study published by Rodriguez-Morales et al., the prevalence of fever was 88.7% (95% CI 84.5–92.9%) (11). In studies by Rodriguez-Morales et al. the prevalence was 89.8% (95% CI 81.8–94.5%) (11). Chang et al. found the prevalence of fever was 59%. Cough is another important clinical symptom in children and a coughing child may act as a carrier of the disease (29). The prevalence of cough was 17.9% (95% CI 17.9 [16.4-19.5]) in the present study. In their meta-analysis study,

Chang et al. showed the prevalence of cough was 46% (29), and Rodriguez-Morales et al. found the prevalence of 57.6% (95% [CI 40.8-74.4%]) (11). In the study by Yang et al., the prevalence of cough was 67.7% (95% CI: 59–76%) (30). Dry cough is not accompanied by sputum and is considered as one of the most important clinical symptoms of COVID-19 disease (31). Nasal discharge and diarrhea are other clinical symptoms of COVID-19. In the present study, the prevalence of nasal discharge and diarrhea was 12.6% (95% CI [11.4-13.9]) and 0.09.5% (95% CI [0.08.1 -1.9]), respectively. In the study of Miri et al. on gastrointestinal problems in COVID-19 patients, the prevalence of diarrhea was 10% and of vomiting 8% (12). The results of a meta-analysis study by Akobeng showed the prevalence of diarrhoea was 12.4% (95% CI 7.8-19.2), vomiting 10.3% (95% CI 4.9-20.3), and the general prevalence of gastrointestinal symptoms 22.8% (95% CI 13.1-35.2) (32).

It is essential to consider gastrointestinal problems in patients with COVID-19 in the diagnosis of COVID-19 based on its clinical symptoms.

4-1. Study Limitation

Articles in Chinese were not included in the study.

5- CONCLUSIONS

Fever, cough, and tachypnea are the most common clinical symptoms of COVID-19. The results of this study can serve as a guide for pediatricians and specialists in the field of infectious diseases to identify the clinical signs of COVID-19 in children and adolescents.

6- ACKNOWLEDGMENTS

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7- CONFLICT OF INTEREST

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Table-1: Specifications of studies entered into the Systematic Review and Meta-Analysis.

	Author, Year, Reference	Age, year	Country	Number of patients	Number of male patients (%)	Number of female patients, Number (%)	Results
1	Dong et al., 2020, (15)	Pediatric	China	2143	1213 (56.6%)	930 (43.4%)	The mean time from onset to diagnosis was 2 days.
2	Xia et al., 2020, (16)	pediatric	China	20	13 (65%)	7 (35%)	Fever and cough were the most common symptoms of the disease.
3	Rahimzadeh et al., 2020, (17)	Children	Iran	9	6 (66.6%)	3 (33.3%)	Fever and cough were present in all patients.
4	Li et al., 2020, (18)	Children	China	5	4 (80%)	1 (20%)	CT scan of all patients was abnormal.
5	Chen et al., 2020, (19)	< 18 years	China	31	13 (41.9%)	18 (58.1%)	There was fever in 14 (45.2%) patients and cough in 13 (41.9%) patients.
6	Cai et al., 2020, (20)	Children	China	10	4 (40%)	6 (60%)	The interval between the onset of symptoms and exposure was 2 to 10 days.
7	Henry et al., 2020, (21)	Children and adolescents	14 Country	82	43 (52.4%)	27 (32.9%)	Fever in 17 (68.0%), Cough in 9 (36.0%), Pharyngitis in 3 (12.0%), Rhinorrhea in 2 (8.0%), Abdominal Pain in 1 (4.0%), Diarrhea in 1 (4.0%), Malaise in 1 (4.0%) and Asymptomatic in 2 (8.0%).
8	Lu et al., 2020, (22)	Children	China	171	104 (60.8)	67 (39.2)	41.5% of children had a fever and 15.8% had no rate of any clinical symptoms.
9	Liu et al., 2020, (23)	Children	China	6	2 (33.33)	4 (66.66)	Hospitalization in the intensive care unit was observed in only one patient. The duration of the fever ranged from 3 to 11 days.
10	Ma et al., 2020, (24)	Children	China	50	28 (56)	22 (44)	Fever was one of the most important symptoms in patients infected with the coronavirus.
11	Liu et al., 2020, (25)	Children	China	4	2 (50)	2 (50)	Clinical symptoms included in Fever, Post-partum fever, Cough, Short of breath, Fatigue, Loss of appetite and Diarrhea.
12	Qui et al., 2019, (26)	Children	China	36	23 (64)	13 (36)	The most important symptoms when admitting these patients are fever and dry cough.
13	Du et al., 2020, (27)	Children	China	14	6 (42.9)	8 (57.1)	The amount of CRP in children was less than adults. The most important symptoms when admitting these patients are fever and dry cough.
14	Sun et al., 2020, (28)	Pediatric	China	8	6 (75)	2 (25)	The most common symptoms of Covid-19 disease in pediatric are polypnea, fever and cough.