Received: 14 October 2021 | Revised: 02 February 2022 | Accepted: 19 February 2022
DOI: 10.22034/ecc.2022.324658.1302
Eurasian Chemical Communications SAMI

FULL PAPER

Chemical laboratory findings in children with covid-19: A systematic review and meta-analysis

Saeideh Azizi Mahkooyeh[a] |Samira Eskandari[b] |Elahe Delavar[c] |Maryam Milanifard[d] |Farzad Esfandiary Mehni[e,*]

[a]*M.Sc in Medical-Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran*

[b]*BSc in Nursing, Islamic Azad University, Tehran Medical Branch, Tehran, Iran*

[c]*M.Sc. Student of Intensive Care Gonabad University of Medical Sciences, Gonabad, Iran*

[d]*Researcher at the Anesthesia and Pain & Molecular and Cell Biology Research Center, Faculty of Medicine, Department of Anatomy, Iran University of Medical Sciences, Tehran, Iran*

[e]*MSc in Nursing. School of Nursing and Midwifery, Jiroft University of Medical Sciences, Jiroft, Iran*

***Corresponding Author:**
Farzad Esfandiary Mehni
Email: Farzad.sfandyary@yahoo.com
Tel.: N/A

Few studies have been performed on the clinical manifestations of COVID-19 in children, and the clinical and laboratory features of children with COVID-19 are challenging, and insufficient evidence has been provided. Therefore, the current study focused on the most prevalent laboratory data in children with COVID-19. In the current study, articles published from January 2019 to December 2021 were reviewed in PubMed, Scopus, Web of Science, and EBSCO databases. For data analysis, after extracting the data of studies that met the inclusion criteria, the effect size was used with a 95% confidence interval; the fixed or random effect model and the Mantel-Haenszel/ REML formula were calculated. Stata software version 16, a faster version of Stata, was used for statistical analysis. A total of 291 articles were found within the starting search, the full text of 52 article were reviewed. Finally, six studies were selected. Most prevalent laboratory findings were 39% decreased White blood cells (95% CI 8%-70%); 36% decreased Lymphocyte (95% CI 5%-67%); 56% increased IL-6 (95% CI 31%-82%); 66% increased Aspartate aminotransferase (95% CI 48%-83%); 49% increased Alanine aminotransferase (95% CI 29%-69%). Current meta-analysis showed in children with COVID-19, the interpretation of laboratory findings is very important and should be given more attention. Early detection of the disease in children can be essential in controlling the COVID19 epidemic, so early detection of important laboratory findings and their increase or decrease can be helpful in early diagnosis.

KEYWORDS

COVID-19; laboratory findings; pediatric; children; SARS-COV-2.

Introduction

COVID-19, which started in China in December 2019 and now affects many countries worldwide, has been formally pronounced a pandemic by the World Health Organization [1]. As of December 17, 2021, there were 5,331,019 deaths and 271,963,258 confirmed cases of Covid-19, for a total of 8,337,664,456 doses of the vaccine [2]. Studies on the virus, the physiopathology of the disease, especially in the final phase, clinical symptoms, course of the disease, laboratory findings, methods of diagnosis, prevention, and treatment are still ongoing, but so far, no specific treatment for the disease has been discovered [3,4]. The disease (Figure 1) can range from a simple infection to acute respiratory failure syndrome. On the other hand, the number of patients in the pre-dangerous phase is relatively high [5].

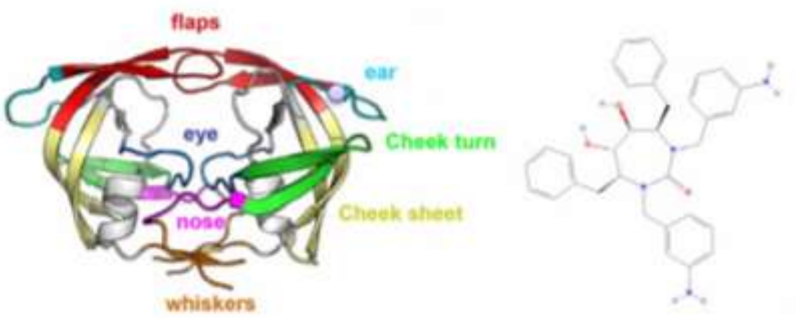

FIGURE 1 Covid formula

It should be noted that children may not be identified in the early stages due to mild clinical symptoms and may be carriers of the disease. With the daily increase in the number of patients worldwide, the prevalence of this disease in children is undoubtedly increasing [6-8]. The most important findings from the analysis of evidence show that children are susceptible to COVID-19, but do not have a recurrent severe illness. Children may facilitate viral transmission [6, 9-11]. Studies have shown that children with COVID-19 have impaired immune function and that normal white blood cell values and absolute lymphocyte counts are lower than normal [12-15]. However, few studies have been performed on the clinical manifestations of children with COVID-19, and the clinical and laboratory features of children with COVID-19 are challenging, and insufficient evidence has been provided. Therefore, the current study focused on the most prevalent laboratory data in children with COVID-19 (Figure 2).

FIGURE 2 Bewildering equation

Method

Search strategy

In this systematic review study, ScienceDirect, Google Scholar, PubMed, Scopus, Web of Science, and EBSCO databases were used to search for articles. In the current study review of previous studies, the PRISMA checklist was used to search for the studies [16]. A software program (Endnote X8) was utilized to manage electronic titles. Selected article filters were performed from January 2019 to December 2021.

Inclusion criteria

Inclusion criteria: children with COVID-19, conventional laboratory indices, laboratory index, age<18 years, Exclusion criteria: experimental studies performed on non-humans, in vitro studies, case studies, reviews, animal studies, and incomplete information.

Data collection and extraction

Data from selected articles were extracted based on years, the number of patients, mean of age, laboratory findings. The studies' quality was assessed using Development and Evaluation (GRADE) guidelines [17]. High scores indicate a low risk of bias, and lower scores indicate low-quality studies. Two blind and independent reviewers extracted the information from the abstract and full content of the articles to extract the data. Before the screening, kappa statistics were performed to confirm the level of agreement between the reviewers with higher kappa values (>0.80).

Data analysis

95 confidence interval (CI) of Effect size with fixed effect or a Random Effect Model and

Mantel-Haenszel or REML procedure were calculated. The random-effects method was employed to assess the potential heterogeneity between studies, and I^2 showed heterogeneity. Random effects were used to deal with potential heterogeneity, and I^2 values showed heterogeneity. I^2 values less than 50% indicate low heterogeneity ($p>0.05$), and high values indicate high heterogeneity ($p<0.05$). Statistical analysis and meta-analysis were performed with Software Version 16 (STATA Corporation).

Result

A total of 291 articles were found in the initial search. After removing duplicates, entry criteria for the titles were applied to the remaining 243 articles, and a summary of the remaining articles was reviewed. In this step, 191 articles were excluded. In the following, the full text of 52 articles were reviewed. Finally, six studies were selected.

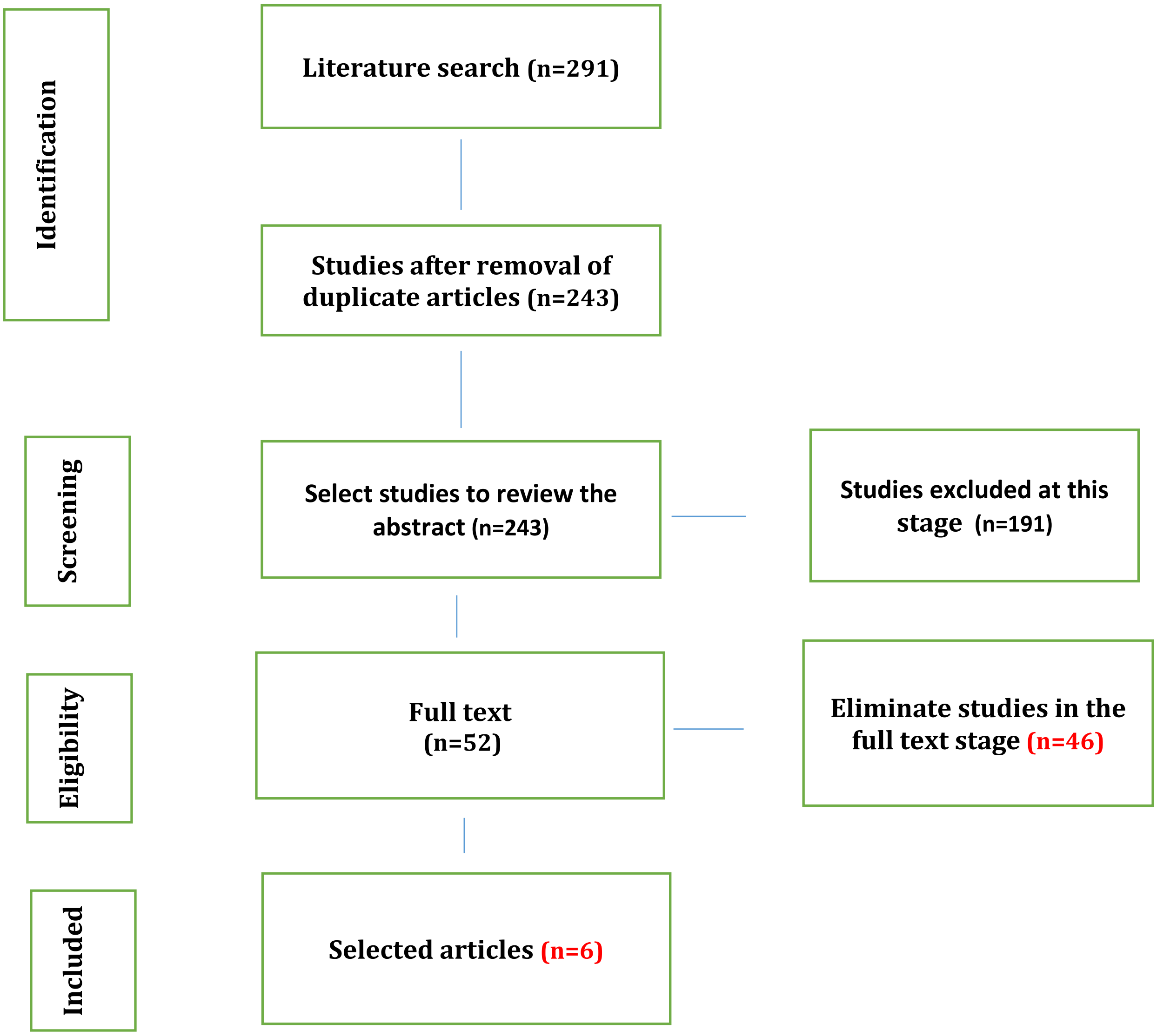

FIGURE 3 Flowchart of the literature search and selection criteria

TABLE 1 Characteristics of Included Studies for meta-analysis

Study. Years	Number of patients		range of age	laboratory findings													
	girls	boys		0↓	1↓	2↓	3↑	4↓	5↑	6↑	7↑	8↑	9↑	10↑	11↑	12↑	13↓
Qiu *et al.*,2020 [18]	13	23	0-16 yr	7	-	11	-	-	3	2	1	1	6	0	3	11	0
Han *et al.*,2020 [19]	3	4	0-17	-	0	0	-	-	3	1	4	2	-	3	-	2	-
Zheng *et al.*,2020 [20]	11	14	2-9	6	-	2	-	-	-	12	19	14	-	-	-	-	-
Su *et al.*,2020 [21]	3	6	1-9	8	-	1	4	-	6	6	6	4	4	4	4	4	-
Liu *et al.*,2020 [22]	4	1	1-13	-	0	1	-	-	-	-	-	4	-	-	-	-	-
Du *et al.*,2020 [23]	8	6	1-17	4	-	-	1	-	1	1	4	1	5	-	5	0	5

0: White blood cells; 1: Leukocyte; 2: Lymphocyte; 3: IL-6; 4: Eosnophils; 5: Aspartate aminotransferase; 6: Alanine aminotransferase; 7: Creatine kinase; 8: C-reactive protein; 9: Procalcitonin; 10: Erythrocyte sedimentation rate; 11: D-dimer; 12: Creatine kinase MB; 13: Oxygen saturation

Characteristics of studies included

Six studies have been included in the present article. The number of patients was 96 (girls: 42 and boys: 54) with a range of age between 1 to 17 years (Table 1).

Bias assessment

According to GRADE, all studies had a low risk of bias and high quality.

Most prevalent laboratory findings

As seen in Figure 2, the most prevalent laboratory findings were 39% decreased White blood cells (95% CI 8%-70%); 36% decreased Lymphocyte (95% CI 5%-67%); 56% increased IL-6 (95% CI 31%-82%); 66% increased Aspartate aminotransferase (95% CI 48%-83%); 49% increased Alanine aminotransferase (95% CI 29%-69%); 49% increased Creatine kinase (95% CI 28%-70%); 50% increased C-reactive protein (95% CI 31%-69%); 32% increased Procalcitonin (95% CI 11%-53%); 29% increased Erythrocyte sedimentation rate (95% CI 1%-57%); 52% increased D-dimer (95% CI 26%-78%); 31% increased Creatine kinase MB (95% CI 11%-51%) with low heterogeneity ($I^2<50\%$; p=0.09).

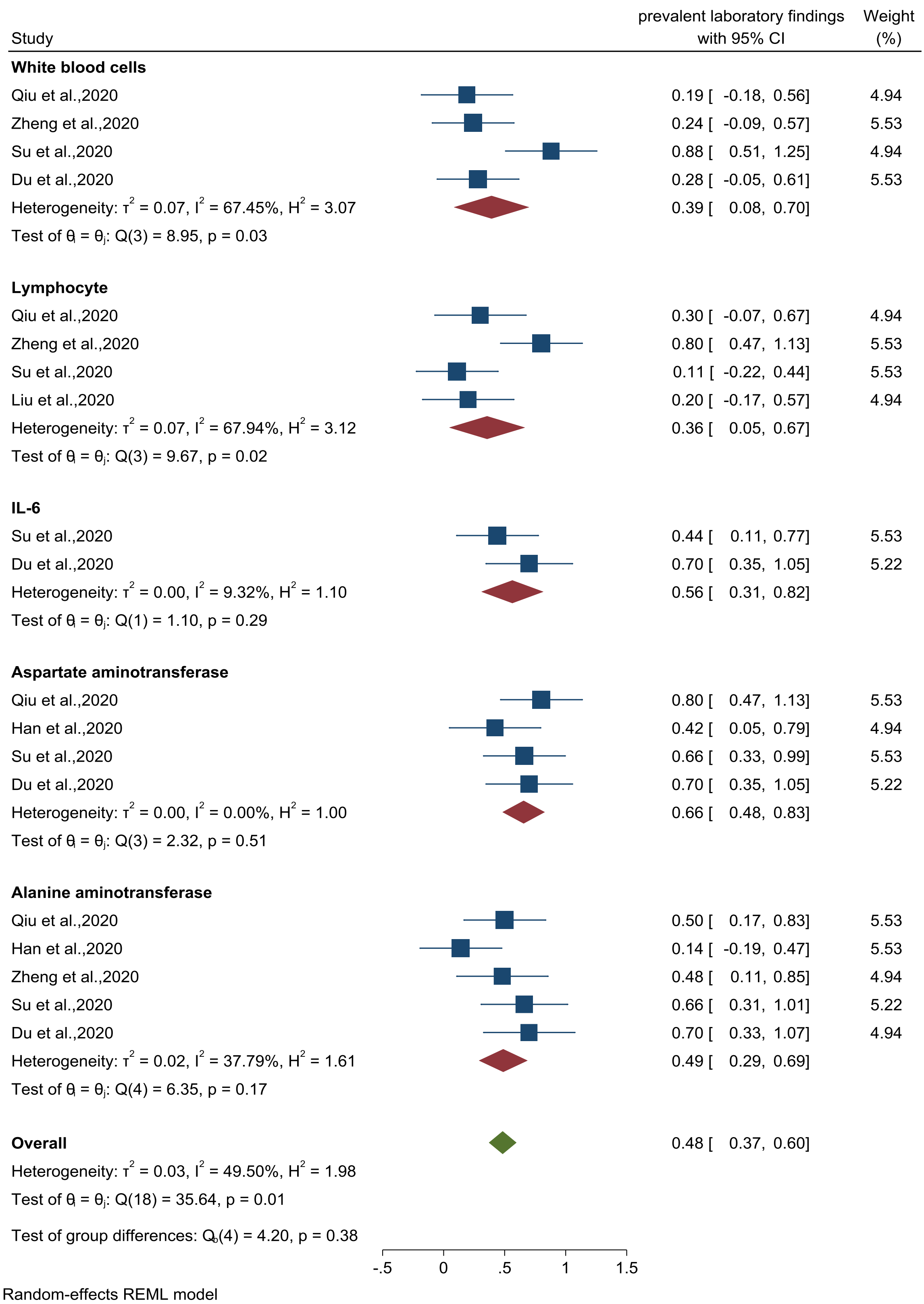

FIGURE 4 The Forest plot demonstrates the most prevalent laboratory data

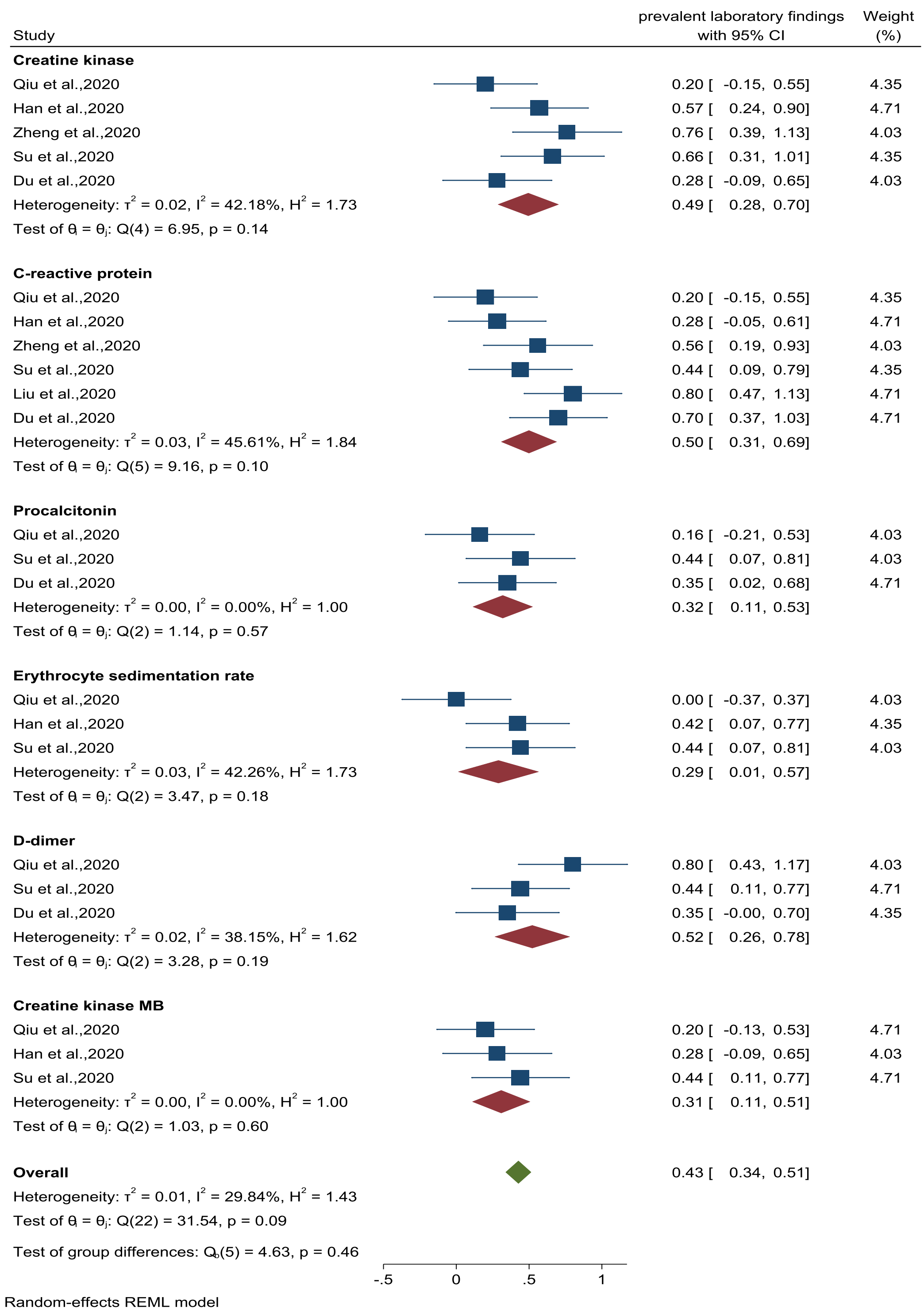

FIGURE 5 The Forest plot showed most prevalent laboratory data

Discussion

Epidemiological, symptomatic, restorative, and preventive foundations have become increasingly important during the Covid-19 epidemic and its worldwide spread. The disease has also had to destroy impacts on the worldwide economy. There is much debate about clinical appearances, laboratory and imaging discoveries, complications, mortality, and severity of the disease, and so far, no specific consensus has been reached. Most studies have been performed on the age group over 18 years because reports indicate that the incidence is higher in this segment of the population and the mortality rate is higher in the elderly. However, the study of this disease in children is also critical [24-27]. The current study aimed at evaluating the most prevalent laboratory data in children with COVID-19. In line with previous studies, the most common laboratory findings showed in figure2 and 3. The results of the studies included in the present study were laboratory findings that were evaluated in confirmed children with COVID-19. There was no high heterogeneity between the study results, in which case the meta-analysis of the present study provides sufficient and robust evidence. However, the limitations of the study should not be ignored.

In the present study, as in all other studies in the pediatric age group, boys were more susceptible to COVID-19 [28-30]. Also, in the older age group, the male population is more prevalent among people with COVID-19, indicating that men are more likely to be COVID-19 than women [31-33]. In general, it can be said that men are more susceptible to COVID-19 in terms of gender. One of the most essential and abnormal laboratory findings in children with COVID-19 was an increase in D-dimer, which needs to be considered in future studies. Current meta-analyses indicate that more comprehensive clinical studies, counting short-term and long-term follow-up cohort evaluations, are still required. Currently, most of the studies are done in China [34]. There is a need for more comprehensive and more studies in other countries to confirm the evidence and to be able to generalize the results to a larger community; because more clinical information is needed to clarify the clinical range of the infection. The clinical findings have been very similar, regardless of the reports to date. Children have a unique role among all human groups because some children do not get it, and if they do, the symptoms are very mild [35]. Of course, it should be noted that children can be carriers, and therefore it is necessary to examine the various cases of children who are infected and hospitalized. Studies have shown that infants and young children are typically at risk for COVID-19. The limitations of the present study were low sample size low available studies. Studies were performed only in China; accurate patient information was not available, clinical results and analysis time, and follow-up period not reported.

Conclusion

Clinical and laboratory findings of Covid-19 disease are more closely related to the course of the disease in adults, and limited data are available in the age group of children. Studies have reported that the course of the disease is milder in children and that conflict with the disease is likely to have a better prognosis in this age group. The current study revealed the most prevalent laboratory findings were decreased Lymphocyte, increased Aspartate aminotransferase (AST), increased Alanine aminotransferase (ALT), increased Lactose dehydrogenase (LDH), increased C-reactive protein (CRP), increased Erythrocyte sedimentation rate, increased D-dimer, decreased Albumin and increased interleukin-6. In children with COVID-19 infection, the interpretation of laboratory data is critical and should be given more attention. Early detection of the disease in children can be essential in controlling the COVID19 epidemic. Therefore, early detection of essential laboratory findings and their increase or decrease can be helpful in early diagnosis.

Acknowledgements

We would like to thank all the people who helped in preparing and compiling the article and collecting the available data.

Orcid:

Saeideh Azizi Mahkooyeh:
https://orcid.org/0000-0002-0080-5269
Maryam Milanifard: https://orcid.org/0000-0002-0888-8847

References

[1] A.M. Milani Fard, M. Milani *Fard, Eurasian J. Sci. Technol.*, **2022**, *2*, 14-31. [Crossref], [Google Scholar], [Publisher]
[2] S. Saedi, A. Saedi, M.M. Ghaemi, M. Milani Fard, *Eurasian J. Sci. Tech.*, **2022**, *2*, 233-241. [Crossref], [Google Scholar], [Publisher]
[3] M. Mokhtare, R. Alimoradzadeh, S. Agah, H. Mirmiranpour, N. Khodabandehloo, *Middle East J. Dig. Dis.*, **2017**, *9*, 228-234. [Crossref], [Google Scholar], [Publisher]
[4] R. Alimoradzadeh, H. Mirmiranpour, P. Hashemi, S. Pezeshki, S.S. Salehi, *Journal of Neurology & Neurophysiology*, **2019**, *10*, 1-5.[Crossref], [Google Scholar], [Publisher]
[5] R. Alimoradzadeh, M.A. Abbasi, F. Zabihi, H. Mirmiranpour, *Iran. J. Ageing*, **2021**, *15*, 524-533. [Crossref], [Google Scholar], [Publisher]
[6] M.B. Abhari, P.F. Afshar, R. Alimoradzadeh, H. Mirmiranpour, *Immunopathol. Persa*, **2019**, *6*, e10. [Crossref], [Google Scholar], [Publisher]
[7] F. Zabihi, MA. Abbasi, R. Alimoradzadeh, *Ann. Rom. Soc. Cell Biol.*, **2021**, 25, 2573-2579. [Pdf], [Google Scholar], [Publisher]
[8] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, D. Altman, G. Antes, D. Atkins, V. Barbour, N. Barrowman, J.A. Berlin, J. Clark, M. Clarke, D. Cook, R. D'Amico, J.J. Deeks, P.J. Devereaux, K. Dickersin, M. Egger, E. Ernst, P.C. Gøtzsche, J. Grimshaw, G. Guyatt, J. Higgins, J.P.A. Ioannidis, J. Kleijnen, T. Lang, N. Magrini, D. McNamee, L. Moja, C. Mulrow, M. Napoli, A. Oxman, B. Pham, D. Rennie, M. Sampson, K.F. Schulz, P.G. Shekelle, D. Tovey, P. Tugwell, *Chin. J. Integr. Med.*, **2009**, *7*, 889-896. [Crossref], [Google Scholar], [Publisher]
[9] Z.L. Zhang, Y.L. Hou, D.T. Li, F.Z. Li, *Scand. J. Cin. Lab. Invest.*, **2020**, *80*, 441-447. [Crossref], [Google Scholar], [Publisher]
[10] W. Alsharif, A. Qurashi, *Radiography*, **2020**, *27*, 682-687. [Crossref], [Google Scholar], [Publisher]
[11] M. Carotti, F. Salaffi, P. Sarzi-Puttini, A. Agostini, A. Borgheresi, D. Minorati, M. Galli, D. Marotto, A. Giovagnoni, *La Radiologia Medica.*, **2020**, *125*, 636-646. [Crossref], [Google Scholar], [Publisher]
[12] A. Zali, M.R. Sohrabi, A. Mahdavi, N. Khalili, M.S. Taheri, A. Maher, M. Sadoughi, A. Zarghi, S.A. Ziai, A.A. Shabestari, M. Bakhshayeshkaram, H. Haghighatkhah, B. Salevatipour, A. Abrishami, M. Raoufi, P. Dehghan, Arash KhamenehBagheri, R. Jalili Khoshnoud, K. Hanani, *Acad. Radiol.*, **2020**, *28*, 1654-1661. [Crossref], [Google Scholar], [Publisher]
[13] P.G. Wasilewski, B. Mruk, S. Mazur, G. Półtorak-Szymczak, K. Sklinda, J. Walecki, *Pol. J. Radiol.*, **2020**, *85*, e361–e368. [Crossref], [Google Scholar], [Publisher]
[14] S. Etemadi, B. Mahmoodiyeh, S. Rajabi, A. Kamali, M. Milani Fard, *Ann. Romanian Soc. Cell Biol.*, **2021**, *25*, 2417-2426. [Pdf], [Google Scholar], [Publisher]
[15] C.R. Jutzeler, L. Bourguignon, C.V. Weis, B. Tong, C. Wong, B. Rieck, H. Pargger, S. Tschudin-Sutter, A. Egli, K. Borgwardt, M. Walter, *Travel Med. Infect. Dis.*, **2020**, *37*, 101825. [Crossref], [Google Scholar], [Publisher]
[16] S.M. Hashemi, M. Hashemi, G. Bahari, A. Khaledi, H. Danesh, A. Allahyari, *Asian Pacific journal of cancer prevention: APJCP*, **2020**, *21*, 2479-2484. [Crossref], [Google Scholar], [Publisher]
[17] S. Saedi, A. Saedi, MM. Ghaemi, M. Milani Fard, *Eurasian J. Sci. Technol.*, **2021**, *2*, 185-196. [Crossref], [Google Scholar], [Publisher]
[18] A. Firoozfar, M. Dousti, *Mag. Civ. Eng.*, **2019**, *90*, 119-129. [Crossref], [Google Scholar], [Publisher]
[19] M.Y. Ng, E.Y. Lee, J. Yang, F. Yang, X. Li, H. Wang, M.M. Lui, C.S. Lo, B. Leung, P.L. Khong, C.K. Hui, *Radiology: Cardiothoracic Imaging*, **2020**, *2*, e200034. [Crossref], [Google Scholar], [Publisher]
[20] C.C. Lai, T.P. Shih, W.C. Ko, H.J. Tang, P.R. Hsueh, *Int. J. Antimicrob.*, **2020**, *55*, 105924. [Crossref], [Google Scholar], [Publisher]
[21] A. Sharma, S. Tiwari, M.K. Deb, J.L. Marty, *Int. J. Antimicrob.*, **2020**, *56*, 106054. [Crossref], [Google Scholar], [Publisher]
[22] A. Tahamtan, A. Ardebili, *Expert Rev. Mol. Diagn.*, **2020**, *20*, 453-454. [Crossref], [Google Scholar], [Publisher]
[23] P.G. Gibson, L. Qin, S.H. Puah, *Med. J. Aust.*, **2020**, *213*, 54-56. [Crossref], [Google Scholar], [Publisher]
[24] F. Fu, J. Lou, D. Xi, Y. Bai, G. Ma, B. Zhao, D. Liu, G. Bao, Z. Lei, M. Wang, *Eur. Radiol.*,

2020, *30*, 5489-5498. [Crossref], [Google Scholar], [Publisher]

[25] Y. Raziani, B.S. Othman, **2021**, *10*, 5-10. [Crossref], [Google Scholar], [Publisher]

[26] S. Ghorbanizadeh, Y. Raziani, M. Amraei, M. Heydarian, *J. Pharm. Negative Results*, **2021**, *12*, 54-58. [Crossref], [Google Scholar], [Publisher]

[27] Y. Raziani, B.S. Othman, S. Raziani, *Ann. Med. Surg. (Lond)*, **2021**, *69*, 102739. [Crossref], [Google Scholar], [Publisher]

[28] Y. Raziani, S. Raziani, *J. Chem. Rev.*, **2021**, *3*, 83-96. [Crossref], [Google Scholar], [Publisher]

[29] A. Susanabadi, S. Etemadi, M.S. Sadri, B. Mahmoodiyeh, H. Taleby, M. Milani Fard, *Ann. Rom. Soc. Cell Biol.*, **2021**, *25*, 2875–2887. [Crossref], [Google Scholar], [Publisher]

[30] R. Alimoradzadeh, M. Mokhtare, S. Agah, *Iran. J. Age.*, **2017**, *12*, 78-89. [Crossref], [Google Scholar], [Publisher]

[31] F.E. Sadr, Z. Abadi, N.E. Sadr, M. Milani Fard, *Ann. Rom. Soc. Cell Biol.*, **2021**, *25*, 6839-6852. [Crossref], [Google Scholar], [Publisher]

[32] H. Jahandideh, A. Yarahmadi, S. Rajaieh, A. Ostvar Shirazi, M.M. Fard, A. Yarahmadi, *J. Pharm. Res. Int.*, **2019**, *31*, 1-7. [Crossref], [Google Scholar], [Publisher]

[33] K. Ghajarzadeh, M.M. Fard, H. Alizadeh Otaghvar, S.H.R. Faiz, A. Dabbagh, M. Mohseni, S.S. Kashani, A.M.M. Fard, M.R. Alebouyeh, *Ann. Rom. Soc. Cell Biol.*, **2021**, *25*, 2457–2465. [Crossref], [Google Scholar], [Publisher]

[34] K. Ghajarzadeh, M. Milani Fard, M.R. Alebouyeh, H. Alizadeh Otaghvar, A. Dabbagh, M. Mohseni, S.S. Kashani, A.M. Milani Fard, S.H.R. Faiz, *Ann. Rom. Soc. Cell Biol.*, **2021**, *25*, 2466-2484. [Crossref], [Google Scholar], [Publisher]

[35] M. Dousti, A. Firoozfar, *J. Eng. Ind. Res.*, **2022**; *3*, 54-68. [Crossref], [Google Scholar], [Publisher]

How to cite this article: Saeideh Azizi Mahkooyeh, Samira Eskandari, Elahe Delavar, Maryam Milanifard, Farzad Esfandiary Mehni*. Chemical laboratory findings in children with covid-19: A systematic review and meta-analysis. *Eurasian Chemical Communications*, 2022, 4(4), 338-346. **Link:** http://www.echemcom.com/article_145173.html