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SYSTEMATIC REVIEW AND META-ANALYSIS OF SERUM AMYLOID A PROGNOSTIC VALUE IN PATIENTS WITH COVID-19

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Abstract

INTRODUCTION: This study was designed to assess the levels of human serum amyloid A (SAA) among COVID-19 patients.

MATERIAL AND METHODS: A systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. A comprehensive literature search was performed (PubMed, Web of Science, Scopus, and Cochrane network), and studies comparing SSA levels in: (A) with non-severe vs severe COVID-19; (B) severe vs critical COVID-19 condition; (C) survived vs died due to COVID-19 in-hospital treatment period — were included. Random-effects meta-analyses were performed to obtain pooled estimates.

RESULTS: Thirty studies met the criteria and were included in the meta-analysis. Pooled analysis showed that SAA levels were statistically significantly lover in non-severe group 58.7 ± 53.9 mg/L compared to 154.5 ± 169.6 mg/L for patients with severe condition (MD = –120.29; 95% CI: –135.35 to –105.22; $p < 0.001$). SAA levels among patients with critical condition were 89.5 ± 90.4 mg/L compared to 195.3 ± 206.2 mg/L (MD = –56.66; 95% CI: –101.81 to –11.51; $p = 0.01$). SAA levels in patient who survived were 108.7 ± 157.3 mg/L, and 206.8 ± 58.8 mg/L for patients who not survived (MD = –85.04; 95% CI: –145.78 to –24.29; $p = 0.006$).

CONCLUSIONS: In conclusion, this updated meta-analysis suggests that SAA concentrations are positively correlated with the severity of the COVID-19. Therefore, SAA can be considered a biomarker for predicting the severity and prognosis of COVID-19. Measurement of this parameter might assist clinicians in monitoring and evaluating the severity and prognosis of COVID-19.

KEY WORDS: serum amyloid A; SAA; marker; SARS-CoV-2; COVID-19; meta-analysis

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INTRODUCTION

According to recent estimations, as of August 11, 2021, there have been about 6 million deaths due to respiratory coronavirus 2 (SARS-CoV-2) [1]. Initially, the global, combined research power of numerous scientists worldwide has focused on developing safe and effective vaccines. Simultaneously, investigators aimed to establish a successful treatment scheme. As new drugs were developed to overcome the acute phase of the disease, the direction of further research has shifted. With growing knowledge about the pathophysiological background, more attention has been brought to the significant heterogeneity of the disease's course, as well as assessing the prognosis of individual patients. Several ongoing studies aimed at determining the prognostic factors, in order to recognize the most vulnerable patients. Therefore, an individually tailored therapy could be suggested. Several biomarkers have been investigated, most of which are associated with the inflammatory state. Other suggested underlying biological pathways may involve endothelial dysfunction, as well as epithelial cell injury. The proposed molecules include IL-6, procalcitonin, ferritin, D-dimer, and C-reactive protein [2]. Some of them have prognostic value, while others reflect the severity of the disease. Marking serum concentrations of such biomarkers may define the subsequent therapeutic approach, as certain levels must be observed in order to initiate specific treatment. Recent studies have highlighted the potential role of another promising biomarker — serum amyloid A (SAA).

SAA is an acute-phase protein, contributing to the deposition of amyloid in tissues, as its precursor. The role of SAA in the pathophysiology of amyloidosis has been well studied [3]. As Covid-19 is associated with an increased inflammatory state, increased levels of certain cytokines can be observed. As a result, the liver is then stimulated to the production of SAA, resulting in its increased concentrations in the acute phase of the disease. However, data regarding the exact clinical value and significance of SAA concentrations in COVID-19 patients remain under investigation.

MATERIAL AND METHODS

The study was designed and performed as a systematic review and meta-analysis and was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines [4].

Study selection

We conducted a computerized search of PubMed, Web of Science, Scopus, and Cochrane network from database inception to April 27, 2022, using the following keywords: "SARS-CoV-2" OR "COVID-19" OR "coronavirus" OR "covid" AND "SAA" OR "serum amyloid A". In addition, a manual search of the included studies and review reference lists on the topic was performed to identify additional eligible studies.

The study included articles indicating SAA levels in patients: (A) with non-severe vs severe COVID-19; (B) with severe vs critical COVID-19 condition; (C) survived vs died due to COVID-19 the in-hospital treatment period. Animal studies, reviews, case reports, letters, conference or poster abstracts, or articles not containing original and not published in English were excluded.

Two reviewers (M.P. and B.F.) independently review each report found by the searching strategy and the results obtained by them were compared and discussed. Potential disagreements were resolved by discussion with a third reviewer (L.S.).

Data extraction

Two reviewers independently perform data extraction. Any disagreements were resolved by discussion with a third author (L.S.). In order to extract the data, the authors used a questionnaire form for the study, which contained data on (A) parametric data of the article (first author's name, year of publication, country of the study, study design); (B) the level of AAS in the patient groups (non-severe vs severe COVID-19 and/or severe vs critical COVID-19 condition and/or survived vs died due to COVID-19).

Additionally, the same reviewers perform the quality assessment of each study. For randomized controlled trials, the revised tool for risk of bias in randomized trials (RoB-2 tool) was used [5]. On the other hand, for non-randomized trials tool to determine the risk of bias in non-randomized studies of interventions was used (the ROBINS-I tool) [6]. The risk of bias assessments was visualized using the Robvis application [7].

Statistical analysis

All analyses will be performed using Stata V.15 (StataCorp, College Station, Texas, USA). The results for dichotomous outcomes were presented as odds ratios (ORs) or risk ratios (RRs) with 95% confidence intervals (CIs). A random-effects model was used to pool study results independently

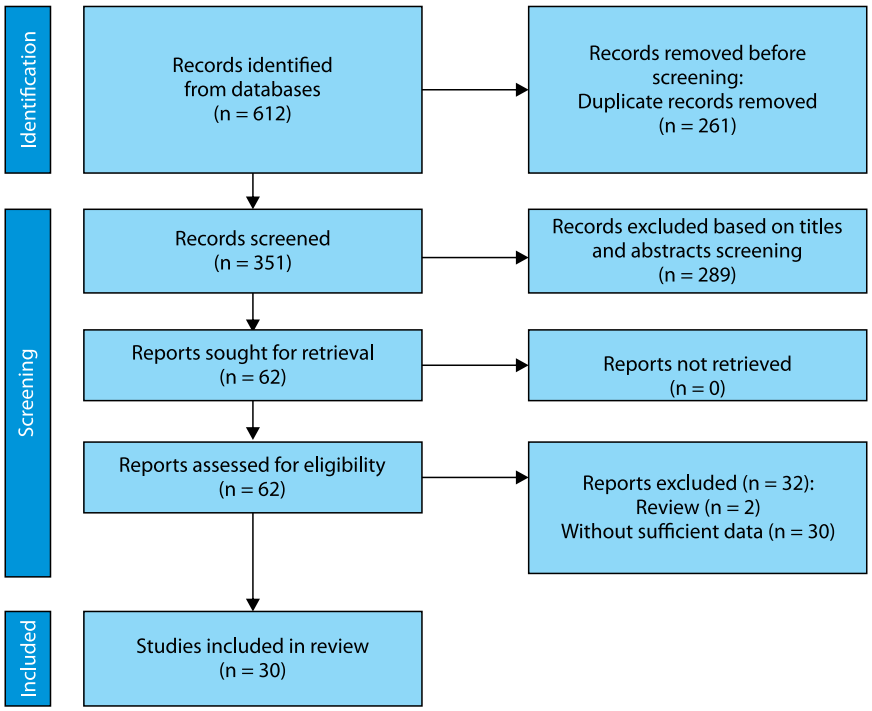

FIGURE 1. Database search and selection of studies according to PRISMA guidelines

of the P-value for heterogeneity or I^2 [8]. All the P-values are two-sided, and a $p < 0.05$ was considered statistically significant. Subgroup analysis will be performed using the Q-test based on ANOVA. We will assess the presence of publication bias using funnel plots and Egger's test [9].

RESULTS

Study selection

Figure 1 depicts the flow diagram for the search process. The initial search retrieved 612 publications. Upon removing duplication and title and abstract screening, 62 were deemed ineligible. The full texts of 62 sources were screened against the inclusion/exclusion criteria. Finally, thirty studies met the criteria and were included in the meta-analysis [10–39].

Among the 30 studies, 28 showed SAA levels in non-severe vs severe COVID-19 patients, six showed SAA levels among severe and critical condition patients, while four had comparisons of survival and non-survival COVID-19 patients. The assessment of their risk of bias is provided in Figures S1–S2 (see Supplementary file).

Meta-analysis

28 studies reported SAA levels in non-severe vs severe COVID-19 patients. Pooled analysis showed that SAA levels were statistically significantly lover in non-severe group 58.7 ± 53.9 mg/L compared to 154.5 ± 169.6 mg/L for patients with severe condition (MD = –120.29; 95% CI: –135.35 to –105.22; $p < 0.001$; Fig. 2).

Six studies reported SAA levels among severe and critical condition patients. Pooled analysis showed that SAA levels among patients with critical condition were 89.5 ± 90.4 mg/L compared to 195.3 ± 206.2 mg/L (MD = –56.66; 95% CI: –101.81 to –11.51; $p = 0.01$; Fig. 3).

Four studies reported SAA levels in patients who survived or died. Pooled analysis showed that SAA levels in patient who survived were 108.7 ± 157.3 mg/L, and 206.8 ± 58.8 mg/L for patients who not survived (MD = –85.04; 95% CI: –145.78 to –24.29; $p = 0.006$; Fig. 4).

DISCUSSION

The initial clinical picture of several patients with COVID-19 is non-specific making the early diagnosis of the disease difficult. The signs and symptoms can range from minimal symptoms and lack of radiological abnormalities to rapid disease progression, ARDS (acute respiratory distress syndrome), and even death [40]. Early identification and prediction of severe patients are of great importance for

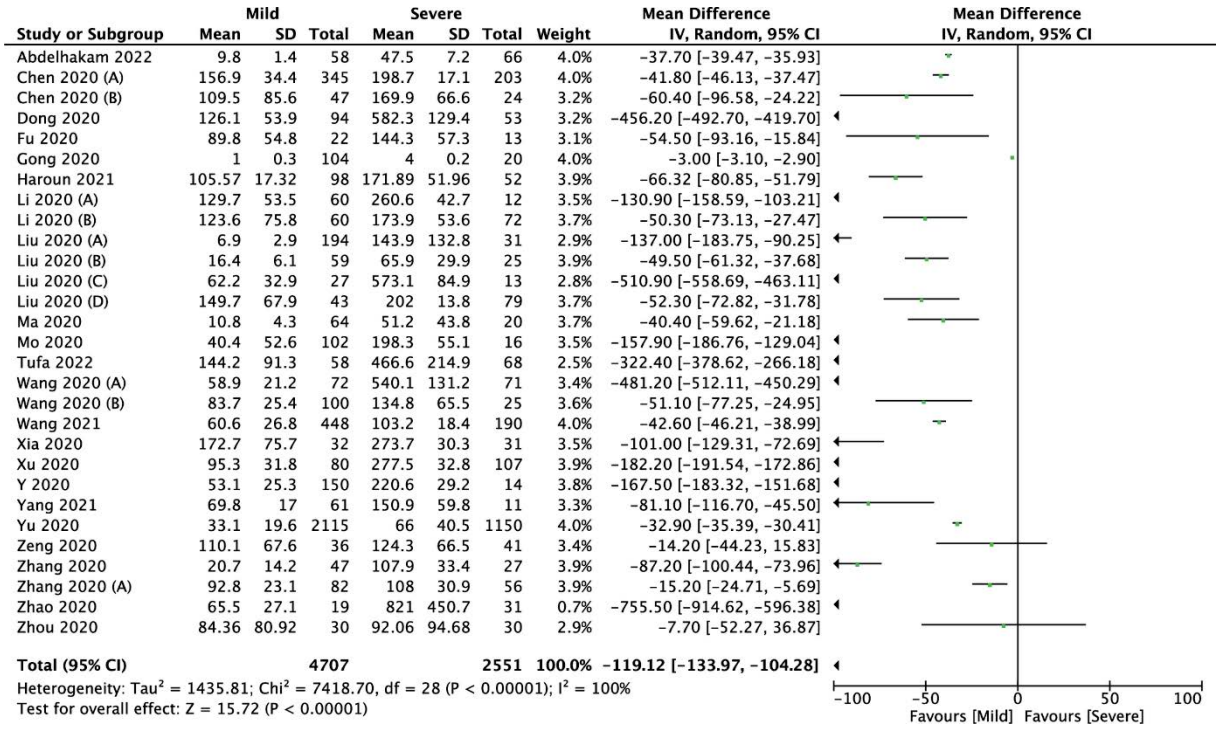

FIGURE 2. Forest plot of SAA levels in non-severe vs. severe COVID-19 groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

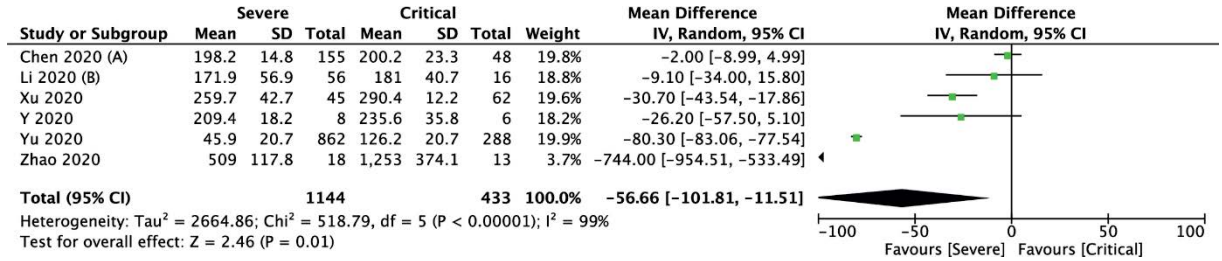

FIGURE 3. Forest plot of SAA levels among severe and critical condition groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

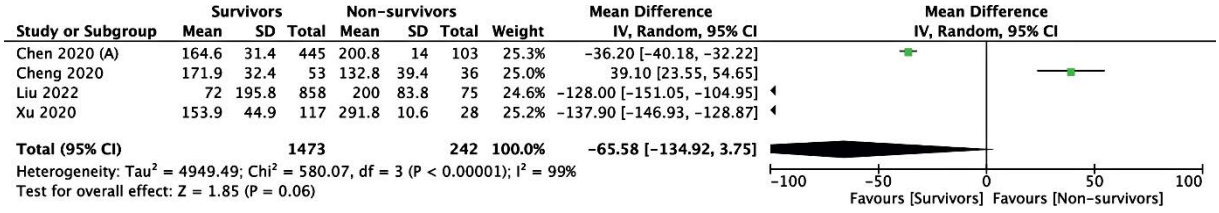

FIGURE 4. Forest plot of SAA levels in patients who survived or died groups. The center of each square represents the weighted standard mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

effectively allocating medical resources and providing adequate interventions to improve the survival chances of patients with COVID-19.

Laboratory indicators can anticipate the progression of the disease and adverse events in COVID-19 patients. SAA is an important potential bi-

omarker that is commonly elevated in the acute phase of inflammatory diseases, mainly viral, and several conditions like obesity, diabetes, liver, and cardiovascular diseases independently associated with significantly worse outcomes in patients with COVID-19 [41].

It has been two years since the World Health Organization declared the COVID-19 pandemic. The purpose of this meta-analysis is to draw updated conclusions about the relationship between changes in SAA levels and the severity and prognosis of COVID-19 patients. Many observational studies have been performed on the relevance of elevated SAA and COVID-19 severity and prognostic value. The first meta-analysis on the associations of a series of inflammatory markers with the severity of COVID-19 published in 2020, highlighted the need for further investigating the association of SAA and the severity of COVID-19, as it included only 3 studies [42].

In our meta-analysis 30 studies involving 8,445 COVID-19 patients were included. 28 studies reported SAA levels in non-severe vs severe COVID-19 patients. Pooled analysis showed that SAA levels were statistically significantly lower in the non-severe group 58.7 ± 53.9 mg/L compared to 154.5 ± 169.6 mg/L for patients with severe conditions. Three previously published meta-analyses investigating SAA in severe vs non-severe COVID-19 patients showed that the SAA of patients with severe COVID-19 was higher than those in the non-severe types of grousp, which is consistent with the pooled results of our meta-analysis. Two of mentioned meta-analyses involved nine studies [43, 44] and one included only five papers [45].

Six studies reported SAA levels among severe and critical condition patients. Pooled analysis showed that SAA levels among patients with the critical condition were 89.5 ± 90.4 mg/L compared to 195.3 ± 206.2 mg/L. Compared to a meta-analysis published in 2021, SAA concentrations were also significantly higher in patients with critical COVID-19 compared with those with severe COVID-19 [46].

Four studies reported SAA levels in patients who survived or died. Pooled analysis showed that SAA levels in patients who survived were 108.7 ± 157.3 mg/L, and 206.8 ± 58.8 mg/L for patients who did not survive. A previous meta-analysis that among 19 involved studies included two studies on survival status in COVID-19 (included also in our meta-analysis) also showed that SAA concentrations were significantly higher in COVID-19 patients with more severe disease and in those who did not survive during follow-up when compared to patients with milder forms of COVID-19 or those who survived during follow-up [47].

Altogether, our meta-analysis suggests that SAA levels can be used to determine COVID-19 severity and prognosis.

The present meta-analysis has some limitations. Firstly, significant heterogeneity of the included studies should be mentioned. There were certain differences regarding the basis for establishing COVID-19 diagnosis among the investigators. Some of the researchers did not include control groups, whereas others did not assess ICU patients. As some of the studies were conducted during the severe period of the epidemic, a considerable number of patients were self-isolating at home and could not be admitted immediately for corresponding treatment. Only a few papers investigated the impact of the examined biomarkers on deaths, therefore data regarding the clinical significance of the acquired findings is scarce. What is more, most of the included papers were single-center experiences. It is worth noting, that some studies included patients with various comorbidities, which themselves may be associated with a poorer outcome of COVID-19. All of these factors may bias the statistical results to some extent.

CONCLUSIONS

In conclusion, this updated meta-analysis suggests that SAA concentrations are positively correlated with the severity of the COVID-19. Therefore, SAA can be considered a biomarker for predicting the severity and prognosis of COVID-19. Measurement of this parameter might assist clinicians in monitoring and evaluating the severity and prognosis of COVID-19.

Authors' contribution

Conceptualization, B.F., and L.S.; methodology, B.F. and L.S.; software, L.S.; validation, B.F., O.Y. and L.S.; formal analysis, M.P. and L.S.; investigation, B.F., M.P., M.C. and L.S.; resources, L.S. and B.F.; data curation, B.F. and L.S.; writing — original draft preparation, B.F., O.Y., A.G., A.S., M.B, and L.S.; writing—review and editing, all authors; visualization, L.S.; supervision, L.S.; project administration, B.F. and L.S.; All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest
The authors declare no conflict.

REFERENCES

1. Simonsen L, Viboud C. A comprehensive look at the COVID-19 pandemic death toll. Elife. 2021; 10, doi: 10.7554/eLife.71974, indexed in Pubmed: 34382937.
2. Tan C, Huang Y, Shi F, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 2020; 92(7): 856–862, doi: 10.1002/jmv.25871, indexed in Pubmed: 32281668.
3. Wilson PG, Thompson JC, Shridas P, et al. Serum amyloid A, but not C-reactive protein, stimulates vascular proteoglycan synthesis in a pro-atherogenic manner. Am J Pathol. 2008; 173(6): 1902–1910, doi: 10.2353/ajpath.2008.080201, indexed in Pubmed: 18974302.
4. Page M, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021: n71, doi: 10.1136/bmj.n71.
5. Sterne J, Hernán M, Reeves B, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016(355): i4919, doi: 10.1136/bmj.i4919.
6. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019; 366: l4898, doi: 10.1136/bmj.l4898, indexed in Pubmed: 31462531.
7. McGuinness LA, Higgins JPT. Risk-of-bias visualization (robvis): an R package and shiny web app for visualizing risk-of-bias assessments. Res Synth Methods. 2021; 12(1): 55–61, doi: 10.1002/jrsm.1411, indexed in Pubmed: 32336025.
8. Welton NJ, White IR, Lu G, et al. The interpretation of random-effects meta-analysis in decision models. Med Decis Making. 2005; 25(6): 646–654, doi: 10.1177/0272989X05282643, indexed in Pubmed: 16282215.
9. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997; 315(7109): 629–634, doi: 10.1136/bmj.315.7109.629, indexed in Pubmed: 9310563.
10. Abdelhakam DA, Badr FM, Abd El Monem Teama M, et al. Serum amyloid A, ferritin and carcinoembryonic antigen as biomarkers of severity in patients with COVID-19. Biomed Rep. 2022; 16(2): 13, doi: 10.3892/br.2021.1496, indexed in Pubmed: 34987797.
11. Bhatraju PK, Morrell ED, Zelnick L, et al. Comparison of host endothelial, epithelial and inflammatory response in ICU patients with and without COVID-19: a prospective observational cohort study. Crit Care. 2021; 25(1): 148, doi: 10.1186/s13054-021-03547-z, indexed in Pubmed: 33874973.
12. Chen R, Sang L, Jiang M, et al. Medical Treatment Expert Group for COVID-19. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. J Allergy Clin Immunol. 2020; 146(1): 89–100, doi: 10.1016/j.jaci.2020.05.003, indexed in Pubmed: 32407836.
13. Chen M, Wu Y, Jia W, et al. The predictive value of serum amyloid A and C-reactive protein levels for the severity of coronavirus disease 2019. Am J Transl Res. 2020; 12(8): 4569–4575, indexed in Pubmed: 32913530.
14. Cheng Li, Yang JZ, Bai WH, et al. Prognostic value of serum amyloid A in patients with COVID-19. Infection. 2020; 48(5): 715–722, doi: 10.1007/s15010-020-01468-7, indexed in Pubmed: 32734556.
15. Dong Y, Zhou H, Li M, et al. A novel simple scoring model for predicting severity of patients with SARS-CoV-2 infection. Transbound Emerg Dis. 2020; 67(6): 2823–2829, doi: 10.1111/tbed.13651, indexed in Pubmed: 32469137.
16. Fu J, Huang PP, Zhang S, et al. The value of serum amyloid A for predicting the severity and recovery of COVID-19. Exp Ther Med. 2020; 20(4): 3571–3577, doi: 10.3892/etm.2020.9114, indexed in Pubmed: 32855710.
17. Gong J, Ou J, Qiu X, et al. A tool for early prediction of severe coronavirus disease 2019 (COVID-19): a multicenter study using the risk nomogram in Wuhan and Guangdong, China. Clin Infect Dis. 2020; 71(15): 833–840, doi: 10.1093/cid/ciaa443, indexed in Pubmed: 32296824.
18. Haroun RAH, Osman WH, Eessa AM. Interferon- -induced protein 10 (IP-10) and serum amyloid A (SAA) are excellent biomarkers for the prediction of COVID-19 progression and severity. Life Sci. 2021; 269: 119019, doi: 10.1016/j.lfs.2021.119019, indexed in Pubmed: 33454365.
19. Li L, Chen C. Contribution of acute-phase reaction proteins to the diagnosis and treatment of 2019 novel coronavirus disease (COVID-19). Epidemiol Infect. 2020; 148: e164, doi: 10.1017/S095026882000165X, indexed in Pubmed: 32713370.
20. Li H, Xiang X, Ren H, et al. Serum Amyloid A is a biomarker of severe Coronavirus Disease and poor prognosis. J Infect. 2020; 80(6): 646–655, doi: 10.1016/j.jinf.2020.03.035, indexed in Pubmed: 32277967.
21. Liu SL, Wang SY, Sun YF, et al. Expressions of SAA, CRP, and FERR in different severities of COVID-19. Eur Rev Med Pharmacol Sci. 2020; 24(21): 11386–11394, doi: 10.26355/eurrev_202011_23631, indexed in Pubmed: 33215460.
22. Liu Q, Dai Y, Feng M, et al. Associations between serum amyloid A, interleukin-6, and COVID-19: A cross-sectional study. J Clin Lab Anal. 2020; 34(10): e23527, doi: 10.1002/jcla.23527, indexed in Pubmed: 32860278.
23. Liu J, Li S, Liu J, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine. 2020; 55: 102763, doi: 10.1016/j.ebiom.2020.102763, indexed in Pubmed: 32361250.
24. Liu J, Tu C, Zhu M, et al. The clinical course and prognostic factors of severe COVID-19 in Wuhan, China: A retrospective case-control study. Medicine (Baltimore). 2021; 100(8): e23996, doi: 10.1097/MD.0000000000023996, indexed in Pubmed: 33663044.

25. Liu N, Long H, Sun J, et al. New laboratory evidence for the association between endothelial dysfunction and COVID-19 disease progression. J Med Virol. 2022; 94(7): 3112–3120, doi: 10.1002/jmv.27693, indexed in Pubmed: 35246853.
26. Ma KL, Liu ZH, Cao CF, et al. COVID-19 myocarditis and severity factors: an adult cohort study. , doi: 10.1101/2020.03.19.20034124.
27. Mo XN, Su ZQ, Lei CL, et al. Serum amyloid A is a predictor for prognosis of COVID-19. Respirology. 2020; 25(7): 764–765, doi: 10.1111/resp.13840, indexed in Pubmed: 32406576.
28. Tufa A, Gebremariam T, Manyazewal T, et al. Cytokine and chemokine profile in patients hospitalized with COVID-19: A comparative study. [preprint]. 2022, doi: 10.1101/2022.03.17.484837.
29. Wang D, Li R, Wang J, et al. Correlation analysis between disease severity and clinical and biochemical characteristics of 143 cases of COVID-19 in Wuhan, China: a descriptive study. BMC Infect Dis. 2020; 20(1): 519, doi: 10.1186/s12879-020-05242-w, indexed in Pubmed: 32677918.
30. Wang R, Pan M, Zhang X, et al. Epidemiological and clinical features of 125 hospitalized patients with COVID-19 in Fuyang, Anhui, China. Int J Infect Dis. 2020; 95: 421–428, doi: 10.1016/j.ijid.2020.03.070, indexed in Pubmed: 32289565.
31. Wang Q, Cheng J, Shang J, et al. Clinical value of laboratory indicators for predicting disease progression and death in patients with COVID-19: a retrospective cohort study. BMJ Open. 2021; 11(10): e043790, doi: 10.1136/bmjopen-2020-043790, indexed in Pubmed: 34598979.
32. Xia X, Wen M, Zhan S, et al. [An increased neutrophil/lymphocyte ratio is an early warning signal of severe COVID-19]. Nan Fang Yi Ke Da Xue Xue Bao. 2020; 40(3): 333–336, doi: 10.12122/j.issn.1673-4254.2020.03.06, indexed in Pubmed: 32376581.
33. Xu Bo, Fan CY, Wang AL, et al. Suppressed T cell-mediated immunity in patients with COVID-19: A clinical retrospective study in Wuhan, China. J Infect. 2020; 81(1): e51–e60, doi: 10.1016/j.jinf.2020.04.012, indexed in Pubmed: 32315725.
34. Yang R, Gui X, Gao S, et al. Clinical progression and changes of chest CT findings among asymptomatic and pre-symptomatic patients with SARS-CoV-2 infection in Wuhan, China. Expert Rev Respir Med. 2021; 15(3): 411–417, doi: 10.1080/17476348.2021.1840358, indexed in Pubmed: 33135909.
35. Yu Y, Liu T, Shao L, et al. Novel biomarkers for the prediction of COVID-19 progression a retrospective, multi-center cohort study. Virulence. 2020; 11(1): 1569–1581, doi: 10.1080/21505594.2020.1840108, indexed in Pubmed: 33172355.
36. Zeng Z, Hong XY, Li Y, et al. Serum-soluble ST2 as a novel biomarker reflecting inflammatory status and illness severity in patients with COVID-19. Biomark Med. 2020; 14(17): 1619–1629, doi: 10.2217/bmm-2020-0410, indexed in Pubmed: 33336592.
37. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020; 75(7): 1730–1741, doi: 10.1111/all.14238, indexed in Pubmed: 32077115.
38. Zhao K, Huang J, Dai D, et al. Serum iron level as a potential predictor of coronavirus disease 2019 severity and mortality: a retrospective study. Open Forum Infect Dis. 2020; 7(7): ofaa250, doi: 10.1093/ofid/ofaa250, indexed in Pubmed: 32661499.
39. Zhou J, Xu XP, Xu F, et al. Clinical symptoms and psychological changes of patients with COVID-19 in Jiangxi Province. [preprint], doi: 10.21203/rs.3.rs-18080/v1.
40. Khan M, Khan H, Khan S, et al. Epidemiological and clinical characteristics of coronavirus disease (COVID-19) cases at a screening clinic during the early outbreak period: a single-centre study. J Med Microbiol. 2020; 69(8): 1114–1123, doi: 10.1099/jmm.0.001231, indexed in Pubmed: 32783802.
41. Zhou Y, Yang Q, Chi J, et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. Int J Infect Dis. 2020; 99: 47–56, doi: 10.1016/j.ijid.2020.07.029.
42. Zeng F, Huang Y, Guo Y, et al. Association of inflammatory markers with the severity of COVID-19: a meta-analysis. Int J Infect Dis. 2020; 96: 467–474, doi: 10.1016/j.ijid.2020.05.055, indexed in Pubmed: 32425643.
43. Mahat RK, Panda S, Rathore V, et al. The dynamics of inflammatory markers in coronavirus disease-2019 (COVID-19) patients: A systematic review and meta-analysis. Clin Epidemiol Glob Health. 2021; 11: 100727, doi: 10.1016/j.cegh.2021.100727, indexed in Pubmed: 33778183.
44. Li Y, Xiaojing He, Zhuanyun Li, et al. Prognostic value of serum amyloid A in COVID-19: A meta-analysis. Medicine (Baltimore). 2022; 101(7): e28880, doi: 10.1097/MD.0000000000028880, indexed in Pubmed: 35363202.
45. Wang L, Yang LuM, Pei SF, et al. CRP, SAA, LDH, and DD predict poor prognosis of coronavirus disease (COVID-19): a meta-analysis from 7739 patients. Scand J Clin Lab Invest. 2021; 81(8): 679–686, doi: 10.1080/00365513.2021.2000635, indexed in Pubmed: 34762008.
46. Zhang D, Huang WJ, Lan MQ, et al. Association between serum amyloid A levels and predicting disase severity in COVID-19 patients: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2021; 25(13): 4627–4638, doi: 10.26355/eurrev_202107_26255, indexed in Pubmed: 34286504.
47. Zinellu A, Paliogiannis P, Carru C, et al. Serum amyloid A concentrations, COVID-19 severity and mortality: an updated systematic review and meta-analysis. Int J Infect Dis. 2021; 105: 668–674, doi: 10.1016/j.ijid.2021.03.025, indexed in Pubmed: 33737133.