

[September 2020 - Volume 13 - Issue 9](#)

- [Previous Article](#)
- **Outline**
 - [Conflict of interest statement](#)
 - [Authors' contributions](#)
 - [REFERENCES](#)
- **Images**
 - [Slideshow](#)
 - [Gallery](#)
 - [Export PowerPoint file](#)
- **Download**
 - [PDF](#)
 - [EPUB](#)
- **Cite**
 - [Copy](#)
 - [Export to RIS](#)
 - [Export to EndNote](#)
- **Share**
 - [Email](#)
 - [Facebook](#)
 - [Twitter](#)
 - [LinkedIn](#)
- **Favorites**
- **Permissions**
- **More**
 - [Cite](#)
 - [Permissions](#)
 - [Image Gallery](#)

Letter to Editor

Lymphopenia as a marker for disease severity in COVID-19 patients

A metaanalysis

Devanandan, Praveen¹; Puvvada, Ranadheer Chowdary¹; Muthukumar, Vijey Aanandhi²,

[Author Information](#)

¹School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, India

¹Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, India

To whom correspondence may be addressed. E-mail: hodpchemistry@velsuniv.ac.in

Received April 16, 2020

Received in revised form July 13, 2020

Accepted July 14, 2020

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Asian Pacific Journal of Tropical Medicine [13\(9\):p 426-428, September 2020](#). | DOI: 10.4103/1995-7645.290588

- Open

Metrics

COVID-19 has become the global focus since December 2019^[1]. Patients usually experience cough, fever and flu-like symptoms. Most patients also experience dyspnoea. Elevated procalcitonin, lymphopenia are observed in COVID-19 patients. Recently, a case series analysis has predicted that lymphopenia may be a very good prognostic marker for disease progression in COVID-19^[2].

An extensive literature search is carried out in PubMed, Scopus and Google Scholar using the medical subject heading terminology (MeSH)-'novel coronavirus', 'ncov-2019', 'Wuhan', 'COVID-19' and 'SARS-CoV-2'. We included papers that reported the epidemiological aspects of COVID-19 such as retrospective studies, observational reports published between 1st January 2020 and 20th March 2020. Papers published in English that reported the biochemical data of these patients were included. Publications with emphasis on severity of the patients were included. Studies that did not report the absolute lymphocyte count, letters to the editor, reviews and opinions were excluded. A meta-analysis was then carried out with the selected studies and individual as well as pooled odds ratio was calculated to determine the statistical importance of lymphopenia on the severity of COVID-19 patients.

Overall 22 articles were identified using our selection criteria, out of which 16 were excluded after reviewing their abstract for full text reading. Six articles provided data of absolute lymphocyte count for all patients as well as for severely ill patients[3-8]. The summarised findings are reported in (Table 1). Two of the articles did not provide data on number of patients who had lymphopenia. Hence 4 manuscripts were finally selected, their individual odds ratio as well as pooled odds ratio was calculated with 95% confidence interval[3678]. The summarised findings are reported in (Table 2) as well as (Figure 1).

Study	Report	Total No. of patients	Absolute Lymphocyte Count (IQR) (x10 ⁹ /L)	Severe outcome	No. of severely ill patients	Absolute lymphocyte count (IQR) (x10 ⁹ /L) severely ill patients
Shang et al[3]	Case report	01	0.80 (0.4-1.1)	ICU Case	01	0.4 (0.2-0.6)
Wang et al[4]	2020	138	0.80 (0.6-1.1)	ICU Case	06	0.3 (0.2-0.4)
Yang et al[5]	Case Report	02	0.74 (0.40-1)	Death	01	0.62 (0.37-1)
Wu et al[6]	Case report	001	1.00 (0.6-1.3)	Death	01	0.6 (0.4-0.8)
Shang et al[7]	Allogeneic (Wuhan)	138	0.80 (0.6-1.1)	Severe	06	0.7 (0.5-1.0)
Zhang et al[8]	2020	1000	1.00 (0.7-1.3)	Severe	150	0.6 (0.4-1.0)

Table 1: Absolute lymphocyte count in COVID-19 patients.

Table 1: Absolute lymphocyte count in COVID-19 patients.

Study	Total No. of patients with lymphopenia	No. of severe cases	No. of severe cases with lymphopenia	OR (95% CI)	P value	Weight (%)
Shang et al[3]	01	01	01	4.77 (0.00-20.17)	0.000	3.20
Wang et al[4]	006	04	00	0.00 (0.00-0.00)	<0.001	17.20
Shang et al[7]	038	006	00	1.90 (0.00-4.10)	0.130	11.05
Fei et al[5]	002	01	01	8.90 (1.76-43.78)	<0.001	70.50
Total	1209	079	001	3.67 (2.39-5.63)	<0.001	100.00

Table 2: Meta-analysis of the available data.

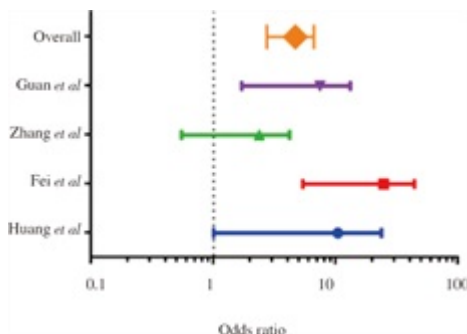


Figure 1: Forest plot of the available data: Odds ratio of the 4 selected studies along with cumulative odds ratio.

From the calculated data, baseline absolute lymphocyte count has a significant impact on the disease severity. A case report reported that patient had a fall in the absolute lymphocyte count even after the initiation of the therapy[9]. The calculated odds ratio suggested a four-fold increase in chance of disease severity (either for ICU care or death) in COVID-19 patients who had a low lymphocyte count at the baseline. In these selected studies, 90.58% (250/276) of the severely ill patients had lymphopenia. This may be a very essential factor in predicting the outcome of the treatment and the course of hospitalization of COVID-19 patients.

The common aetiology of lymphopenia is auto-immune disorders (such as rheumatoid arthritis, myasthenia gravis), carcinomas, infectious diseases like AIDS, tuberculosis and inherited conditions like ataxia-telangiectasia, and Wiskott-Aldrich syndrome. Chemotherapeutic agents may also cause lymphopenia. In the selected studies, totally 13 patients had carcinoma of various nature[368] 2 patients reported immunodeficiency[8] and 2 patients reported secondary pulmonary tuberculosis[7]. Among these only 3 cancer patients and 2 pulmonary tuberculosis patients reported for severe COVID-19 outcome[78]. Even if the data of these patients are not considered, the resulting odds ratio is 3.67 (95% CI 2.39 to 5.63).

Lymphopenia is commonly observed in severe acute respiratory syndrome (SARS) as well as Middle East respiratory syndrome (MERS) although the cause of lymphopenia in these diseases is unknown. Studies reported that SARS CoV virus may lead to T cell depletion by directly infecting T cells; however, there are contraindicated studies which emphasized on the role of cytokine induced cell death as well as bone marrow hematopoietic progenitor cells suppression. It was observed from a study that delayed clearance of SARS coronavirus from the lung tissue was associated with reduced pulmonary recruitment of lymphocytes is seen in mice^[10]. Additional studies are essentially needed to confirm whether lymphopenia could be a predictable marker for projecting the disease severity.

It could be observed that the absolute lymphocyte count is comparatively lesser in the severely ill patients as well as non-survivors. We sorted out 4 studies that reported on number of patients who had lymphopenia among all patients as well as severe cases^[3678].

The combined odds ratio calculated based on weight of each study is indicating extremely significant ($P < 0.001$) outcome. The test for heterogeneity $I^2 = 73\%$. An odds ratio above 1 is considered significant for the predicted outcome. The overall calculated odds ratio is 3.98 which indicates almost 4 times higher chance for the predicted outcome (Disease Severity in COVID-19 patients).

In conclusion, there is a 4-fold higher risk of disease severity either ICU care or death in patients who have a low lymphocyte count at the baseline. Low lymphocyte count may affect drug selection. Hence, lymphopenia maybe a very essential factor in predicting the outcome of the treatment and the course of hospitalization of COVID-19 patients.

Conflict of interest statement

We declare that we have no conflict of interest.

Authors' contributions

P.D. developed the hypothesis, P.D., R.C.P conducted literature search. P.D, R.C.P., M.V.A carried out analytical calculations and writing of the manuscript. M.V.A is the supervisor.

REFERENCES

[1]. Lu H, Stratton C, Tang Y. Outbreak of pneumonia of unknown etiology in Wuhan China: the mystery and the miracle J Med Virol. 2020;92(4):401–402

- [Cited Here](#)

[2]. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang Yi, et al Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study Sig Transduct Target Ther. 2020;33(5) doi:10.1038/s41392-020-0148-4.

- [Cited Here](#)

[3]. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China The Lancet. 2020;395(10223):497–506

- [Cited Here](#)

[4]. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China JAMA. 2020 doi:10.1001/jama.2020.1585.

[5]. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study The Lancet. 2020 doi:10.1016/S2213-2600(20)30079-5.

[6]. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study The Lancet. 2020;395(10229):1054–1062

- [Cited Here](#)

[7]. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China Allergy. 2020 doi:10.1111/all.14238.

- [Cited Here](#)

[8]. Guan WJ, Ni ZY, Hu Y, Liang W, Ou C, He J, et al Clinical Characteristics of Coronavirus Disease 2019 in China N Engl J Med. 2020 doi: 10.1056/NEJMoa2002032.

- [Cited Here](#)

[9]. Zhang Z, Li X, Zhang W, Shi Z, Zheng Z, Wang T. Clinical features and treatment of 2019-nCov pneumonia patients in Wuhan: Report of a couple cases Virol Sin. 2020;35(3):330–336

- [Cited Here](#)

[10]. Chen J, Lau YF, Lamirande EW, Paddock CD, Bartlett JH, Zaki SR, et al Cellular immune responses to severe acute respiratory syndrome coronavirus (SARS-CoV) infection in senescent BALB/c mice: CD4+ T cells are important in control of SARS-CoV infection J Virol. 2010;84:1289–1301

- [Cited Here](#)

[View full references list](#)

© 2020 Asian Pacific Journal of Tropical Medicine | Published by Wolters Kluwer – Medknow

[View full article text](#)

Related Articles

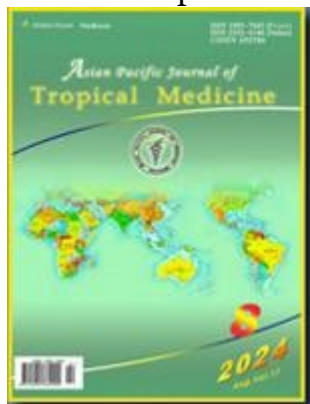
- [Association between serum albumin levels and disease severity in adult patients with dengue](#)
- [Prevalence of cryptosporidiosis in animals in Iran](#)
- [Evaluation of parasitemia by qPCR in patients with chronic Chagas disease treated with benznidazole](#)

- [Association between the Lung Immune Prognostic Index and mortality in patients with idiopathic inflammatory myopathy-associated interstitial lung disease](#)
- [Perceived susceptibility, severity, and reinfection of COVID-19 may influence vaccine acceptance](#)
- [Perceived susceptibility, severity, and reinfection of COVID-19 may influence vaccine acceptance-Authors' reply](#)

Most Popular

- [Medicinal and biological potential of Thuja occidentalis](#)
- [Role of doxycycline in the treatment of dengue infection: An open-label, randomized, controlled, pilot trial](#)
- [Diagnostic performance of C-reactive protein level and its role as a potential biomarker of severe dengue in adults](#)
- [Inappropriate antibiotic dispensing and use](#)
- [Nigella sativa oil as a treatment for gingivitis](#)

[^Back to Top](#)



Never Miss an Issue

Get new journal Tables of Contents sent right to your email inbox

Browse Journal Content

- [Register on the website](#)
- [Get eTOC Alerts](#)

Customer Service

- [Browse the help center](#)
- Contact us at:
 - Support:
[Submit a Service Request](#)
 - TEL:
800-638-3030 (within the USA)
301-223-2300 (outside of the USA)

[Manage Cookie Preferences](#)

- [Privacy Policy](#)
- [Legal Disclaimer](#)
- [Terms of Use](#)
- [Open Access Policy](#)
- [Your California Privacy Choices](#)



- Copyright © 2024
- Asian Pacific Journal of Tropical Medicine | Published by Wolters Kluwer - [Medknow](#)