International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 600-605 www.ijdmsrjournal.com ISSN: 2582-6018

A Novel Hematological Prognostic Index for Covid 19 Severity – A Comparison between the Young and the Old in a Tertiary Care Hospital.

Dr Christina Avril Goveas , Dr Priyadharshini B, Dr Chandrashree J, Dr Ankit Pandey

Senior Resident , Dept of Pathology, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India.
Senior Resident , Dept of Pathology, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India.
Post graduate, Dept of Pathology, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India.
Senior Resident , Dept of respiratory medicine, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India.

Submitted: 01-08-2021 Revised: 08-08-2021 Accepted: 11-08-2021

ABSTRACT

Objectives : To develop a new simple hematological prognostic index (severity index) in order to assess the severity state of SARS-CoV-2 at the earliest.

To compare the hematological prognostic index between the young and old and to correlate it with the clinical severity of the disease.

Materials and Methods:

This observational cross sectional study was conducted in all the covid 19 positive patients, as well as in patients who were tested negative for covid, but with positive CT findings favouring a diagnosis of covid 19,in both young and old(n=250 , each group) . The clinical symptoms and the lab parameters such as total wbc count, LDH, Absolute Monocyte and absolute lymphocyte count were analyzed to calculate the prognostic index, which was compared with the clinical severity in both the age groups. Statistical analysis was computed by kappa statistics, chi square test, t test and one-way anova test.

Results : The prognostic index (severity index) was found to be statistically significant among both the age groups ($p<0.001$) and was also found to be directly proportional to the clinical severity of the disease.

Conclusion: The prognostic index can be used to predict the clinical outcome and severity in patients with covid-19 during early stage of the disease.

Keywords: Covid-19, Severity Index, LDH, SARS-CoV-2

I INTRODUCTION

COVID 19 was declared as a pandemic by the WHO on the 11th march 2020 and has caused the most dangerous health disaster throughout the world since the second world war(1).

In India, around 10 million people have been infected and approximately 150 thousand people have succumbed to SARS-CoV-2 infection(2).

Covid 19 infection presents as a range of symptoms comprising of fever, cough, sore throat, myalgia on the milder side of the spectrum to pneumonia and ultimately respiratory failure on the severe side of the spectrum(3).

Many studies on prognostic indices have been conducted and analysed, namely the biomarkers such as Serum ferritin, lactate dehydrogenase, Creactive protein, procalcitonin, IL6, D dimer(4,5).

As the second wave has caused increased mortality and morbidity among covid 19 patients, with the extensive pressure on the already overburdened intensive care units, the time has come to find out ways to understand and categorise the severity of the disease at the earliest time of presentation, by studying a novel haematological prognostic index(7).

No studies regarding the index have been done in the Indian Population and hence the need for the study.

II MATERIALS AND METHODS

Source of data:

With the approval of the Institutional Ethical Committee (Date 30/6/2021, protocol number: SIMS/IEC/629/2021-22), All the laboratory tested covid 19 positive patients (tested by either Rapid antigen test /RTPCR) and the covid 19 negative patients with positive CT findings suggestive of covid 19 infection, admitted in the McGann District teaching Hospital Shimoga, were included in the study.

Sample size:

In each group, a sample size of 250 were included.

Since the comparison is between the

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 600-605 www.ijdmsrjournal.com ISSN: 2582-6018

young and the old patients, the young patient's category were taken between the age group 18 to 45 years (Group 1) and the old patient's category were taken above the age of 45 years (group 2).

Design of the study:
Observational cross-sectional study.

Inclusion Criteria:
1. All the laboratory tested covid 19 patients admitted to the hospital, irrespective of the comorbidities in the patients.
2. All the patients tested negative for covidwith positive CT findings suggestive of covid.

Exclusion criteria:
1. Pregnant patients
2. Pediatric patients
3. Patients who died within few hours of admission, especially when their hematological parameters have not been analyzed.
4. Patients with symptoms of covid 19 with negative RTPCR/ RAT reports and negative CT changes.

Methodology:
The Clinical features and lab parameters of all the laboratory tested covid 19 patients, admitted to McGann District teaching HospitalShimogawere studied.
The clinical features were assessed by history taking and the remaining data were retrieved from the case sheets. It was categorized / staged as follows:[7, 8]
-Mild (Clinical Symptoms with absent radiographic features)
-Moderate (Respiratory symptoms with CT changes)
-Severe (RR>30/min or SpO2 < 93%)
-Critical (Ventilator support)

For the laboratory work up:The blood sample was assessed by Sysmex (automated cell counter). From the hematological parameters, total WBC count, monocyteand lymphocyte count were studied. LDH was the only biochemical parameter which was analyzed.Thehematological prognostic index or the severity index is calculated according to the following formula: Monocyte/lymphocyte absolute counts x LDH (lactate dehydrogenase)/upper normal LDH value This new index is the result of 3 main parameters which are the monocyte count, lymphocyte count and lactate dehydrogenase which is the enzyme reflecting the disease severity[7].

The prognostic index was classified as mild if it was below 0.60, moderate if it was between 0.60 and 1.55, and more than 1.55 for severe cases.

After calculation of the prognostic index in each group, the prognostic index was correlated with the clinical stagein both the age groups to see the statistical significance. The index was also correlated with the clinical outcome as well.

Statistical analysis:
The data collected wasanalyzed by kappa statistics, chi square test, t test and one-way anova test. The p value <0.05 was considered to be statistically significant.

III RESULTS

A total of 250 patients were studied in each group.The severity index/hematological prognostic index was compared with the clinical stage, separately in each group, by kappa statistics and the p value was found to be statistically significant (p =0.000)

Table 1: Distribution of the young and the old patients as per the severity index and clinical stage

Age group	Severity index category	Clinical stage Mild	Clinical stage Moderate	Clinical stage Severe	Clinical stage Critical	Total
Young	Mild (<0.66)	37	36	92	16	181
	Moderate (0.6 to 1.55)	2	10	32	5	49
	Severe (>1.55)	0	4	12	4	20
	Total	39	50	136	25	250
Old	Mild (<0.66)	13	50	67	11	141
	Moderate (0.6 to 1.55)	3	14	37	5	59
	Severe (>1.55)	2	14	22	12	50
	Total	18	78	126	28	250

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 600-605 www.ijdmsrjournal.com ISSN: 2582-6018

Chi square test to compare the variation in the young and the old in terms of the categorical variables

The **age group when compared with the severity index** yielded a significantp value (p=0.000), i.e., the severity index was more with the age.

Cross tabulation of **age and clinical stage** was significant (p=0.002) implying that clinical stage of disease increases with age.

Table 2 :Independent t test was done to compare the variables among the different age groups

	Young age, Mean ± sd	Old age, Mean ± sd	t	P value
Age	36.04±7	61.28±9.61	-33.569	**<0.001**
LDH	909.66±512.89	1179.73±902.45	-4.114	**<0.001**
Monocyte percentage	2.12±1.85	2.02±1.64	0.639	0.523
Absolute Monocyte Count	165.54±171.96	179.88±190.11	-0.885	0.377
Total WBC Count	8022.72±3987.19	9149.04±5720.82	-2.554	**0.011**
Absolute Lymphocyte Count	1274.32±762.69	1173.57±1053.24	1.225	0.221
Lymphocyte percentage	18.6±10.48	15.04±10.84	3.73	**<0.001**
Severity Index calculation	0.53±0.83	1.11±1.88	-4.503	**<0.001**

LDH comparisonbetween the two groups showed that LDH is higher in Older age group and is statistically significant with a p value of <0.001.

Analysis of the Monocyte and the Lymphocyte percentage among the two groups showed that both were found to be higher in the Younger age group , but the former was not statistically significant and the latter was statistically significant.

Total WBC Count and the severity Index calculation was found to be higher in Old aged group with a statistically significant result.

Table 3 :Chi square test to compare the severity index in the young and the old age group with the clinical outcome

		Value	df	P value (<0.05 is significant)
Young age	Pearson Chi-Square	26.984	2	**<0.001**
Old age		4.014	2	.134

Table 4 :Overall comparison of Lactate dehydrogenase with the clinical stage

LDH	Clinical Stage	numbers	Mean	SD	df2(welch) / F(Anova)	p value
	Mild	57	613.0737	347.8464		
	Moderate	128	1027.142	814.1959		
	Severe	262	1066.24	719.0392	162.955	**<0.001**
	Critical	53	1444.774	787.3652		
	Total	500	1044.694	745.6057		

Table 5 :Overall comparison of the monocyte percentage with the clinical stage

Monocyte percentage	Clinical Stage	numbers	Mean	SD	df2(welch) / F(Anova)	p value
	Mild	57	2.473684	2.236908		
	Moderate	128	2.325781	1.706645		
	Severe	262	1.962977	1.632677	139.31	**0.02**
	Critical	53	1.584906	1.669108		
	Total	500	2.074	1.74751		

International Journal Dental and Medical Sciences Research
Volume 3, Issue 4, July-Aug 2021 pp 600-605 www.ijdmsrjournal.com ISSN: 2582-6018

Using one way ANOVA test to analyse the monocyte percentage yielded the following result -mean value of Mild (2.473684) is highest followed by Moderate(2.325781),Severe(1.962977) least in Critical(1.584906). This difference is statistically significant.

Table 6 :Overall comparison of the lymphocyte percentage with the clinical stage

Lymphocyte percentage	Clinical Stage	Numbers	Mean	SD	df2(welch) / F(Anova)	p value
	Mild	57	23.68421	12.87184		
	Moderate	128	17.32813	10.58978		
	Severe	262	16.28244	10.01044	144.146	**<0.001**
	Critical	53	10.88679	8.558982		
	Total	500	16.822	10.79454		

Comparison of Lymphocyte percentage using one way ANOVA test showed that the mean value of Mild (23.68421053) is highest followed byModerate (17.328125), Severe(16.28244275) least in Critical(10.88679245). This difference is statistically significant.

Table 7:Overall comparison of the severity index with the clinical stage

Severity Index	Clinical Stage	numbers	Mean	SD	df2(welch) / F(Anova)	p value
	Mild	57	0.380456	0.836318		
	Moderate	128	0.847836	1.603681		
	Severe	262	0.800137	1.429455	154.82	**0.001**
	Critical	53	1.340057	1.818726		
	Total	500	0.821736	1.482462		

Comparison of Severity Index calculation using one way ANOVA test showed that the mean value of Critical (1.340057) is highest followed by Moderate (0.847836), Severe (0.800137) least in Mild(0.380456). This difference is statistically Significant.

IV DISCUSSION

As we all know, the covid 19 pandemic has caused enough mortality and morbidity throughout the world. The patients who are affected by the disease, may recover or may succumb to it, due to the varying nature of the disease.

In order to detect the disease at an earlier stage, a prognostic index was developed by Hammadi et al, with the index comprising of the absolute monocyte and lymphocyte count, LDH.

Other scoring systems have been devised with various other lab parameters,to predict the mortality of covid 19. Some of them being the covid 19 lab score and CoLACD[9,10]. Other studies have compared CT scores and laboratory parameters[11].

This particular prognostic index called the covid severity Iraqi index by Hammad et al, is a new one of its kind, with basic, routine parameters to evaluate the severity of the disease at an early stage. No other articles have been published in this regard. Both the clinical features(which can be graded) and the lab parameters can supplement each other in diagnosis and predicting the severity of the disease.

In our study, the prognostic index was calculated and compared with the clinical stage in both the young and the old age groups, and the result was found to be significant (p value of <0.05), implying that the critical clinical stage is directly proportional to the severity index.

The severity index was also found to be more in the old age group as compared to the young.

As far as the individual parameters are concerned, in our study, the LDH values shoots up with severity the disease. Thefinding of this parameter is consistent with the studies done byMoutchia et al, Taj et al, Garcia et al,Han et al, to name a few[13,14,15].

In our study, the lymphocyte count decreased with the severity and with age(Lymphopenia) and was found to be statistically significant (p<0.001). This finding is in concordance with the studies done byDevanandan et al, Antunez et al, Zhang et al to name different studies[10,11,16].

Lymphopenia in covid is predominantly due to the inflammatory cytokine storm[17]. Other mechanisms could be due to the result of selective bone marrow suppression of the lymphocytes or due to redistribution of the cells.

Similarly, monocytopenia is also a consistent feature seen in severe covid 19 infection, which was the finding in our study as well as in studies done by Anurag et al[18].

Every study has its own merits and limitations. Merits being that : this study is one of a kind, with the routine parameters being the components of the severity index.So, the results are easy to calculate and interpret.Moreover, the results of the correlation of the severity index with the clinical stage of the disease,published in the reference article by Hammad et al as well asours, are statistically significant.

The limitations of this study are that, the other lab parameters like procalcitonin, IL2, IL- 6, D dimer and crp and Ct score were not included as components of the index.

In conclusion –our data and the statistical analysis of the same shows a statistical significance between the clinical stage of the disease and the severity index, and between age and severity index as well, thereby making it a good index to assess the severity of covid 19.

Also, to the best of our knowledge ,these studies have not been done in the Indian Population, hence the reason to do the same. But further validation in large cohort is required.

Acknowledgement : My sincere thanks to Dr Priyadharshini B for the idea and concept to conduct this study and Mr Sreekanth for his amazing work as a statistician.
Conflict of interest : None

REFERENCES

[1]. WHO. Statement on the second meeting of the International Health Regulations (2005) EmergencyCommittee regarding the outbreak of novel coronavirus (SARS-CoV-2). Available at:https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(SARS-CoV-2).

[2]. Wikipedia. COVID-19 pandemic data. Availableonline: https://en. wikipedia.org/ w/index.php? title=Template:COVID-19_pandemic_data&oldid=989520654.

[3]. Huang, C., Wang, Y., Li, X., et al. Clinical features of patients infected with 2019 novelcoronavirus in Wuhan, China. The lancet. 2020 Feb 15;395(10223):497-506.PMID: 31986264

[4]. Zhou, F., Yu, T., Du, R.,et al.Clinical course and risk factors for mortality of adultinpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet.2020; 395: 1054–1062.PMID: 32171076

[5]. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. Jama.2020 Apr 28;323(16):1545-6.DOI: 10.1001/jama.2020.4031

[6]. Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19). 2021 Apr 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 32150360.

[7]. Hammadi A, Al Jubouri A, Ahmed G,et al.A New Hematological Prognostic Index For Covid-19 Severity. 2021medRxiv 2021.02.11.21251285; doi: https://doi.org/10.1101/2021.02.11.21251285 (Preprint)

[8]. China National Health Commission. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial version 7) 2020 [cited 2020 17 Apr]. Available from: http://busan.china-consulate.org/chn/zt/4/P020200310548447287942.pdf.

[9]. Antunez Muiños, P. J., López Otero, D., Amat-Santos,et al.The COVID-19 lab score: an accurate dynamic tool to predict in-hospital outcomes in COVID-19 patients. Scientific Reports. 2021;11:9361doi: 10.1038/s41598-021-88679-6.

[10]. AntunezMuiños, P. J., López Otero, D., Amat-Santos,et al. The impact of charlson comorbidity index on mortality from SARS-CoV-2 virus infection and A novel COVID-19 mortality index: CoLACD. Int J Clin Pract. 2020;00:e13858. https://doi.org/10.1111/ijcp.13858

[11]. Zhang, B., Zhang, J., Chen, H.,et al.Novel coronavirus disease 2019 (COVID-19): relationship between chest CT scores and laboratory parameters. European Journal of Nuclear Medicine and Molecular Imaging. 2020;47(9):2083-2089. doi: 10.1007/s00259-020-04854-3 [Epub ahead of print]PMCID: PMC7215122

[12]. Moutchia J, Pokharel P, Kerri A,et al.Clinical laboratoryparameters associated with severe or critical novelcoronavirus disease 2019 (COVID-19): Asystematic review and meta-analysis. PLoS ONE15(10): e0239802. doi :10.1371/journal.pone.0239802

[13]. Taj S, kashif A, Arzinda Fatima S, et al. Role of hematological parameters in the stratification of COVID-19 disease severity. Annals of Medicine and Surgery. 2021;62:68-72.doi :10.1016/j.amsu.2020.12.035

[14]. Wendel Garcia, P. D., Fumeaux, T., Guerci, P.,et al.Prognostic factors associated with mortality risk and disease progression in 639 critically ill patients with COVID-19 in Europe: Initial report of the international RISC-19-ICU prospective observational cohort. EClinicalMedicine. 2020;25:100449.DOI10.1016/j.eclinm.2020. 100449

[15]. Han, Y., Zhang, H., Mu, S.,et al.Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. Aging. 2020;12(12):11245-11258. https://doi.org/10.18632/aging.103372 PMID: 32633729

[16]. Devanandan P, Puvvada RC, Muthukumar VA. Lymphopenia as a marker for disease severity in COVID-19 patients: A meta-analysis. Asian Pac JTrop Med 2020; 13(9): 426-428.doi: 10.4103/1995-7645.290588

[17]. Tavakolpour S, Rakhshandehroo T, Wei E, Rashidian M. Lymphopenia during the COVID-19 infection: What it shows and what can be learned. Immunology Letters. 2020;225:31-32. doi: 10.1016/j.imlet.2020.06.013PMID: 325 69607

[18]. Anurag A, Jha P, Kumar A. Differential white blood cell count in the COVID-19: A cross-sectional study of 148 patients. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(6):2099-2102.doi: 10.1016/j.dsx.2020.10.029PMID: 33160224