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ORIGINAL ARTICLE

Lymphopenia is Associated with Severe Coronavirus Disease 2019 (COVID-19) Infections

MARIA SHIREEN[1], SARAH SHOAIB QURESHI[2], ARSALAN NAWAZ[3], WASIM AMIR[4], MEHRIN FAROOQ[5], S. KHURRAM S. KAZMI[6]

[1]Senior Registrar, Department of Medicine, Lahore Medical and Dental College, Lahore.
[2,4]Professor of Medicine, Lahore Medical and Dental College, Lahore.
[3]Assistant Professor of Medicine, University of Lahore, Lahore.
[5]Associate Professor of Medicine, Lahore Medical and Dental College, Lahore.
[6]Professor of Medicine, Lahore Medical and Dental College, Lahore.

Correspondence to Dr Maria Shireen, Email ID: mariadoc85@yahoo.com, Phone: 0323-4930341

ABSTRACT

Background: Covid-19 is a very contagious and quickly spreading viral infection, caused by a corona virus SARS-COV-2 which was originally reported in China on December 5, 2019. It was confirmed as pandemic by WHO on March 11, 2020. This disease is yet under research. It has variable severity which includes no symptoms to pneumonia. This can cause death of the patient.
Aim: To evaluate the association of Lymphopenia with severity of COVID 19 in COVID-19 patients
Methods: It was a retrospective observational study conducted in COVID wards of Ghurki hospital Lahore. Record of 100 COVID-19 patients that were admitted between March and July 2021 fulfilling the inclusion criteria was included in the study. A pre-structured pro forma was filled to collect the data.
Results: Out of 100 patients, 30 patients were included in Non-severe group while severe group had 70 patients. The mean age of study population was 52.5±10.38 with 60% male and 40% female. 70% patients in severe group had some co-existent comorbidity. The most commonly reported symptoms were fever and cough in both groups while shortness of breath was more commonly reported in severe group.
Conclusion: Lymphopenia is associated with severe Coronavirus disease 2019 (COVID-19) infections. Lymphocytes count can be used to assess the severity of COVID 19.
Keywords: Lymphocytes, Lymphopenia, Coronavirus disease 2019, COVID 19.

INTRODUCTION

Coronavirus pandemic started in Wuhan, China in December 2019. This severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) is similar to SARS like coronaviruses previously reported in bat[1,2]. This disease is called Corona virus disease 2019 (COVID-19). As of 3rd September 2021, 218 946 836 confirmed, and 4 539 723 mortality cases were reported to the World Health Organization[3]. In Pakistan according to NCOC 1171578 cases have been reported and 260354 mortality cases were reported[4].

COVI19 is spread by respiratory droplets and contact with infected body fluids and secretions so it can spread easily from person to person[5,6]. The symptoms vary from mild illness to moderate to severe disease leading to ventilator support[1]. The symptoms of COVID-19 consist of dry cough, fever, lethargy, myalgia, pneumonia, and acute respiratory distress syndrome. There can also be diarrhea, septic shock, metabolic acidosis, coagulation profile derangement and failure of organs including heart, kidney, and liver failure[7,8,9].

Baseline examinations comprise of complete blood count, biochemical tests and coagulation profile. The biochemical tests include renal and liver function, creatinine kinase, lactate dehydrogenase, ferritin and electrolytes[8]. Out of these tests, complete blood count is the easily assessable and cost-effective. It can help in early identification of severe cases, immediate treatment, and supportive care. The early identification of COVID severity helps to reduce mortality[1].

Coronaviruses are single-stranded RNA viruses.[11 12] Before the COVID-19 pandemic, in the previous two decades, two highly lethal coronaviruses causing diseases were documented named severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV)[13]. Natural killer cells and cytotoxic T cells are the main components in control of viral infection[1].

The lymphocyte count is very important in COVID 19. It has been linked with severity of COVID-19. [14] More severe cases have lower lymphocyte count than less severe cases. The recent COVID-19 investigators, have also focused on the clinical significance of lymphopenia as a prognostic marker for COVID-19 patients.

While few studies have been conducted regarding lymphopenia and its association with severity of COVID 19, only a handful can be attributed to medical research professionals of Pakistan. Thus the current study was conducted. The aim of study was to evaluate the association of Lymphopenia with severity of COVID 19 in COVID-19 patients.

METHODS

This retrospective observational study was conducted at COVID wards Medicine Unit of Ghurki hospital Lahore treating COVID-19 patients from April 2021 to July 2021. After permission from review board, informed consent was

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deferred due to retrospective and observational character of this study. Anonymity and confidentiality was ensured. A pre structured proforma was filled to collect the data. Hospital record was studied. A data of 100 patients was acquired. Patients with age > 18 years and positive COVID-19 RT PCR for nasopharyngeal swab specimens were included in study.

Patients with fever or other respiratory symptoms like cough and shortness of breath, typical CXR abnormities of COVID 19 and positive RT-PCR for SARS-CoV-2 RNA was included in non-severe group. While patients with above mentioned symptoms, Respiratory rate > 30 per minute and oxygen saturation <94% were included in severe group. Patients with COVID symptoms but negative PCR were excluded.

Data collection: A pre structured pro forma was filled to collect the data. Demographic details, clinical symptoms and laboratory findings including CBC, TLC, DLC, CRP, serum ferritin, D dimers, LDH, liver function tests, renal function tests were attained from medical records.

Data analysis: Data were entered and analyzed with IBM SPSS 23. Mean and standard deviations were evaluated for quantitative variables like age of patient. p- value ≤ 0.05 was termed significant based on the application of post stratification Chi Square Test.

RESULTS

Record of 100 COVID-19 patients was included in the study. Non-severe group included 30(30%) patients while severe group included 70(70%) patients. The mean age was 52.5±10.38. Out of 100 patients 60(60%) were male while 40(40%) were female. Out of which, 40(66.7%) male were in severe group while 20(33.3%) were in non- severe group. For female 10(25%) were in non-severe and 30(75%) were in severe group. (Table 1)

In this study 60% patients which were in severe group had some co-existent comorbidity. Fever was reported in 20(26.7%) in non-severe group and 55(73.3%) in severe group. Cough was reported in 25(29.4%) in non-severe group and 60(70.6%) in severe group. Shortness of breath was more commonly reported in severe group (100%). (Table 2)

Non severe and severe groups 250 (U/L) for LDH, 150 (ng/mL) for ferritin, 0.5 (ng/mL) for D dimer, 1500 10^3/µL lymphocytes was compared on the basis of being above the normal cut-off values as shown in table 2.

Severe group showed high CRP (86.7%) as compared to non-severe group. D-dimer and ferritin was also raised in severe group. Lymphocytes <1500 10^3/µL were more reported in severe group (100%). P value is less than 0.05 which is significant showing association between lymphocytes and COVID severity as shown in table 3.

Analysis of gender of patient and severity of Covid

Gender	Severity of Covid		Total
	Non severe	**Severe**	
Male	20	40	60
Female	10	30	40
Total	30	70	100

Analysis of symptoms of patient and severity of Covid

		Severity of Covid		P-value
		Non severe	**Severe**	
Fever	Yes	20(26.7%)	55(73.3%)	0.208
	No	10(40%)	15(60%)	
Cough	Yes	25(29.4%)	60(70.6%)	0.760
	No	5(33.3%)	10(66.7%)	
Shortness of breath	Yes	0	70(100%)	0.000
	No	30(100%)	0	
Comorbidity	Yes	0	60(100%)	
	No	30(75%)	10(25%)	

Analysis of investigations and severity of covid

		Severity of covid		*p*-value
		Non severe	**Severe**	
CRP >5mg/dl	Yes	10(13.3%)	65(86.7%)	0.000
	No	20(80%)	5(20%)	
D. dimer >0.5 ng /ml	Yes	10(13.3%)	65(86.7%)	0.000
	No	20(80%)	5(20%)	
LDH >250U/L	Yes	5(11.1%)	40(88.9%)	0.000
	No	25(45.4%)	30(54.5%)	
Ferritin >150ng/ml	Yes	3(6.25%)	45(93.75%)	0.000
	No	27(52%)	25(48%)	
Lymphocytes <1500 (10^3/ul)	Yes	0	60(100%)	0.000
	No	30(75%)	10(25%)	

DISCUSSION

COVID 19 has spread worldwide that has affected billions of people causing loss of human life. Research showed that in severe cases there is increased morbidity and mortality as compared to non-severe group so early identification of the disease is needed[15,16,17].

Researchers had done numerous studies in past couple of years to identify the prognostic factors of COVID-19 severity. One of them is lymphopenia. Analysis showed lymphopenia was linked with severe COVID19, ARDS, increasing mortality and so the poor prognosis[18]. Definition of Lymphopenia, we took in our study is <1500 10^3/µL.

In this study 60% patients in severe group had some co-existent comorbidity. All patients with comorbidity were in severe group. In both groups Fever and cough were the most commonly reported symptoms while shortness of breath was more commonly reported in severe group (100%). Severe group showed high CRP (86.7%) as compared to non-severe group. D-dimer and ferritin was also raised in severe group. Definition of Lymphopenia, we took in our study is lymphocytes <1500 10^3/µL. Lymphocytes <1500 10^3/µL were more reported in severe group. P value is also significant showing association of lymphopenia with disease severity. Lymphopenia showed positive relationship with co-morbidity, CRP, D-dimer, LDH and Ferritin. It was worth mentioning that everyone with Lymphocytes <1500 10^3/µL was in severe group.

Analysis showed lymphopenia was linked with severe COVID19, ARDS, increasing mortality and so the poor prognosis. [18] The factors used in severity criteria have direct association with decrease lymphocyte count like shortness of breath, increase respiratory rate, decrease saturation, more oxygen requirement, prolonged hospital stay and higher mortality. Other makers were also raised more with disease severity including CRP, ferritin, LDH and D-Dimers. So these are also used to see severity and also help in modification in treatment.

Jongmin Lee described in his study that Lymphopenia is linked with severe Coronavirus disease 2019(COVID-19) infections[11]. Ian Huang said in his study that Patients with severe COVID-19 had lower lymphocyte count compared to non-severe COVID-19 patients ($p < 0.001$)[14]. Qianwen found that lymphopenia was associated with threefold increased risk of severe COVID-19[18], Liu Y, Liu W, Wang D, Zhang J, Guan W found the similar association between lymphopenia and COVID 19 severity[19,20, 21,22,23].

Lymphocytes play an essential role in keeping immune homeostasis and inflammatory response in the body. There are few probable mechanisms causing lymphopenia in COVID 19 infection. (1) Direct injury from virus (2) Lymphatic organs might affected by virus like spleen causing lymphocyte destruction (3) Inflammatory cytokines like tumor necrosis factor (TNF)α and interleukin (IL)-6 can also be a factor causing decreased lymphocytes[7,18].

So the lymphocytes count can be used to assess the severity of COVID 19. Lymphopenia is associated with disease severity.

CONCLUSION

Lymphopenia is associated with severe Coronavirus disease 2019(COVID-19) infections. Lymphocytes count can be used to assess the severity of COVID 19.

Conflict of interest: None

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