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ORIGINAL ARTICLE

Lymphopenia is an indicator of severity of the disease and predicts mortality in COVID-19.

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ABSTRACT… Objectives: To assess the impact of lymphopenia on the COVID-19 disease outcome. **Study Design:** Retrospective study. **Setting:** ICU and Isolation Ward of Hayatabad Medical Complex, Peshawar. **Period:** July 2020 to Dec 2020. **Material & Methods:** Different parameters of CBC were performed using the five parts Sysmex differential hematology analyzer BS-1800. A total of 274 patients were included via non probability sampling. Relevant information's were recorded on a pre-designed performa prepared in accordance with the objectives of the study. **Results:** The absolute lymphocyte count was lower in patients who were admitted in ICU as compared to those in isolation ward (p-value 0.07). Likewise patients with severe lymphocytopenia (lymphocyte count less than 50x10*9/L) had a greater rate of mortality (p value 0.01). No significant difference in term of TLC and ANC was noted in survivor's vs non survivors groups in present study. **Conclusion:** Our study concludes that lymphopenia serves as a reliable and early prognostic factor in determining disease severity and mortality COVID-19.

Key words: COVID-19, Lymphopenia, Mortality.

INTRODUCTION

The first pneumonia cases of unknown origin were identified in Wuhan, China in December, 2019.[1] The pathogen was being identified as an enveloped RNA virus, structurally belonging to family of beta-coronavirus. It was being named as severe acute respiratory syndrome coronavirus 2 (SARS-COV2), being similar to SARS-COV phylogenetically.[2]

Number of COVID-19 patients is drastically increasing and all the critical patients need treatment in intensive care units (ICU) causing a major challenge to health sectors. For timely triaging of patients, an early recognition of severe forms of COVID-19 is absolutely required.[3] Older age and co-morbidities pose an increased risk of deaths; however younger adults without any major co-morbidities are also reported to present with complications.[4]

Globally a total of 103,135,836 cases have been reported worldwide with 2,229,456 deaths 31st Jan 2021. In Pakistan, by 31st Jan 2021, a total of 544,813 confirmed cases with 11,657 deaths have been reported. 465000 cases have been recovered and 1316 cases are under treatment. Khyber Pukhtunkhwa the corona cases crossing 66,953 cases with 1848 deaths.[5]

Quantitative abnormalities in hematological indices in CBC reports are used for assessment of prognosis, in order to know the impact of the COVID-19 on hematopoietic system and homeostasis which significantly suffer the outcome in this deadly disease.[6]

Increasing scientific research in field of COVID-19, the abnormalities in routine laboratory investigations, particularly the baseline investigations that is complete blood picture, has the potential to indicate the severity of the

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disease in a quick, easy, affordable, accessible and economical way and can give a way forward for the specific tests for diagnosis and prognosis of the disease.[7,8] Other studies revealed a high leukocyte count in COVID-19. ICU patients with severe complications with median peak ANC and lymphopenia as compared to non-ICU patients without complications ($p<0.001$).[9,10]

Lymphopenia has been shown to present as a common feature of COVID-19, the causes of which could be multiple; it has been shown that lymphocytes express ACE-2 receptors on their surface, thus predisposing them to be attacked by the virus and ultimately causing lysis of lymphocytes Activation of lymphocytes my also induce atrophy of lymphoid organs including spleen, which further disturbs turnover of lymphocytes.[11]

Lymphocyte count less than 20% and chest CT scan findings with more than 50% involvement might be related to the patient's mortality.[12]

Present study was therefore designed as to assess the impact of the hematological markers on the COVID-19 disease outcome. This will help in identifying patients at high risk and vigilant care could be provided to those within our limited resources.

MATERIAL & METHODS

This Retrospective Cohort Study was conducted from July 2020 to Dec 2020 in ICU and isolation wards of at Hayatabad Medical Complex, Peshawar.

A total of 274 patients were included via non probability sampling. All patients whose PCR reports were available were included in the study.

Written informed consent was taken from all patients who were to be included. Real Time PCR was performed was performed at pathology laboratory of Hayatabad Medical Complex, Peshawar. Complete blood counts were done using sysmex analyser.

COVID-19 patients where deficient readings were available on chart of patients, or patients expired before to be fully investigated were excluded. Similarly all patients with any type of symptoms came to emergency or outdoor patients department or even confirmed patients of COVID-19 in emergency units or cold wards not yet entered in isolation department or COVID ICU were also excluded.

This study was conducted in line with the research regulations, followed the sound medical practice, redetected human rights and also within the principles of declaration of Helsinki of World Medical Association. Ethical endorsement was obtained from the institutional ethical review board of Post-Graduate Medical Institute, Hayatabad Medical Complex via letter No- 49/Path/HMC Dated 04/02/2022.

Sampling size of 274 was calculated to represent the true population using the anticipated proportion of associated factors of mortality due to COVID-19 at 5% with abnormal hematological markers at 95% confidence level and 5% absolute precision.[13]

Data was entered in the SPSS version 25 for analysis. Numerical variables like age, Hb% (g/dl), TLC (x10.e3/ul), ANC (x10.e3/ul), ALC (x10.e3/ul), NLR, Platelet count were presented with Mean and Standard Deviation. Student t-test was used to find the difference of the hematological markers in groups of discharged versus expired patients. Chi square test was used to show the impact of the lymphocyte and plate count on mortality in COVID-19. A p-value of less than 0.05 was taken as significant.

RESULTS

A total of 274 patients admitted with SARS-COV2 at Hayatabad medical complex between March 2020 and June 2020. The study population was predominantly males. Total number of male patients was 200 (73%) while that of females was 74(27%).

A total of 52 patients (19%) were admitted to ICU while 222 (81%) did not need ICU admission. The Mean age with SD was 41+ 9 years.

The Mean with SD of Hb%, TLC and Platelet is shown in Table-I. The mean ALC was lower in patients requiring ICU admission anytime during their period of hospitalization as compared to those who got discharged without the need for ICU admission (p-0.07) Table-II. There was a significant association of lymphopenia with mortality in COVID-19 (p-0.01) (Table-III).

Description	HB (g/dl)	TLC ($x10^3$ /ul)	PLT ($x10^3$/ul)
Number of patients	274	274	274
Mean	13.29	12.82	246.54
Median	13.40	11.85	232
Std. Deviation	6.09	5.853	112.179
Range	103.5	34	639
Minimum	2.5	1	9
Maximum	106	36	648

Table-I. Descriptive statistics.

Admission Status		N	Mean	Std. Deviation	Std. Error Mean	P-Value
TLC (x10.e3/ul)	Isolation ward	226	12.67	5.902	0.393	0.8
	ICU	48	13.51	5.628	0.812	
Group Statistics						
Admission Status		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P-Value**
ANC (x10.e3/ul)	Isolation ward	226	10.27	5.949	0.396	0.9
	ICU	48	11.53	5.663	0.817	
Group Statistics						
Admission Status		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P-Value**
ALC (x10.e3/ul)	Isolation ward	226	1.30	0.972	0.065	0.07
	ICU	48	0.96	0.565	0.082	
Group Statistics						
Admission Status		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P-Value**
NLR	Isolation ward	226	14.13	20.440	1.360	0.56
	ICU	48	16.93	13.080	1.888	

Table-II. Difference of TLC/ANC/ALC in ICU and isolation ward patients.

Impact of lymphocyte count					
Outcome	**Lymphocytopenia (x10×9/L)**			**Total**	**P-Value**
	1- 1.5	**0.5 to 1**	**less than 0.5**		
Satisfactorily discharged	134	64	46	244	0.01
Expired due to COVID-19	8	9	11	28	
Total	142	73	57	272	
2. Impact of Platelet count					
Outcome	**Thrombocytopenia (x10×9/L)**			**Total**	**P-value**
	101-150	**50-100**	**less than 50**		
Satisfactorily discharged	16	12	216	244	0.42
Expired due to COVID-19	4	2	22	28	
Total	20	14	238	272	

Table-III. Impact of the lymphopenia and thrombocytopenia on mortality in COVID-19.

DISCUSSION

The impact of the hematological markers on mortality is less studies in our set up. The easy and cost effective test like CBC can give you valuable information, statistically proves to have a significant outcome on the mortality in COVID-19.[14] The data in Pakistan is scarce to support the evidence. In this study we have analyzed different parameters of CBC in relation with disease severity and mortality. Patients admitted in ICU were reported to have lower absolute lymphocyte count as compared to those

admitted in isolation wards (p-0.07). Likewise is reported from other studies conducted in China where they have reported an association of 3 fold increase in disease severity and mortality with sever lymphopenia.[15]

We observed a significant difference ($p<0.05$) in the NLR values (High ANC and low ALC) of the CBC report in the both groups under study Other researcher finding do support the fact that NLR is diagnostic and prognostic marker in viral infections.[16] Ai-Ping Yang et al reported NLR with AUC of 0.743 on ROC to determine the outcome of the seriously ill patients due to COVID-19 to document the prognostic values of Lymphopenia.[17]

We observed a significant number of patients expired who had severe lymphocyte count as compared to those who had mild lymphocytopenia (p value <0.01). This supports the results done in a study which showed a 12 fold increase in mortality in patients associated with severe lymphocytopenia.[18]

A local study published in Pakistan Journal Of medical Sciences reported that Lymphopenia was present in 6.9% of total patients. Significant association was found between lymphopenia and disease severity as well as lymphopenia and mortality (< 0.001). Lymphopenia was found to be a predictor of disease severity using regression analysis (<0.001).[19] Besides that Numerous studies globally have been reported with keen interest in the Lymphocyte count for the clinicians due to its economical availability and as it is an immunological finding in patients infected with corona virus and may be used as a prognostic marker to predict outcome in covid-19.[20,21,22]

CONCLUSION

Hence it was concluded that that lymphopenia serves as a reliable and early prognostic factor in determining disease severity and mortality COVID 19.

There were some limitations of the study. Smaller sample size restricts us to predict the application of this study on larger population. Studies executed with larger sample size can estimate the true population impact. Therefore it is suggested that future studies should cover large population with representation to predict/suggest the findings for decision makers.

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2	Ayesha Sarwar	Writing manuscript, Critical review.	
3	Khalid Khan	Data collection, Data analysis.	
4	Hamzullah Khan	Designed study, Data analysis critical review.	
5	Shahtaj Khan	Design of study, critical review.	
6	Ansa Rehman	Data collection, Data analysis.	
7	Huma Riaz	Data collection and analysis.	