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Evaluation of Hematological, Coagulation and Inflammatory Parameters in COVID-19 in a Tertiary Care Setting of Sindh, Pakistan

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ABSTRACT

Objective: COVID-19 is caused by SARS-CoV-2. Although pulmonary manifestations have been identified as the major symptoms, several hematological abnormalities play a vital role in disease treatment and monitoring. This study summarizes the hematological abnormalities (platelets, white blood cells, hemoglobin, coagulation alterations) as well as changes in inflammatory markers.

Study Design And Setting: A retrospective cross-sectional study was conducted among PCR positive COVID-19 patients. The study was conducted at pathology department of CMH Malir between Aug 2021 and Jan 2022.

Methodology: All the individuals with positive real-time reverse transcription-polymerase chain reaction (PCR) results were involved in the study. One hundred and twenty six COVID-19 patients were included using convenience sampling. Six ml venous blood was collected and analyzed. The data were entered and analyzed using SPSS version 23.

Results: Among 126 patients different hematological and inflammatory parameters were noted. Significantly raised CRP, ESR in 96.8% and 92.9 % were noted respectively. Other parameters like raised D-dimers was found in 60.3 %, leukocytosis 65.1%, neutrophilia in 62.7 %. Significantly elevated neutrophil lymphocyte ratio was seen in 62 % of patients. Parameters like anemia and prolonged PT / APTT were not significant.

Conclusion: The study concluded that CRP, ESR, leukocytosis, neutrophilia, elevated Neutrophil to lymphocyte ratio and D-dimers are significantly raised among serious patients with COVID-19 disease and can be used as monitoring, prognosis and severity index.

Keywords: COVID-19, hematological parameters, neutrophil to lymphocyte ratio.

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INTRODUCTION:

December 2019 was the beginning of a new era in the medical world, when the world was hit by an outbreak of cluster of pneumonia cases. The cause was found out to be a novel corona-virus. It was formally designated as COVID -19 by WHO in Feb 2020, and name of the virus was decided as severe acute respiratory syndrome corona-virus 2 (SARS-COV-2).

It was highly contagious among close contacts and in two months it was spread to the whole world affecting 213 countries. It was declared as the deadliest pandemic in the history affecting more than 253 million and causing 5 million deaths till Nov 2021.[3]

In Pakistan around 1.53 million confirmed cases of COVID-19 have been reported with 30,379 deaths so far.[4] COVID-19 is a multiorgan disease affecting pulmonary, cardiovascular, neurological, musculoskeletal, gastrointestinal and hematological system. It is a very diverse disease and shows a magnitude of symptoms of varying severity. Some patients remain asymptomatic while others develop severe life-threatening complications resulting in death.[5] Good patient management requires early diagnosis, isolation and

risk stratification of patients.[6]

COVID-19 significantly affects the hemostasis and the hematopoietic system. The PCR is the gold standard investigation for diagnosing covid but it is not widely available specially in villages and far flung areas of developing country like Pakistan. In this setting, one of the commonest and earliest investigation advised for the suspected COVID-19 patients is complete blood count (CBC). It is easiest, quickest, widely available and one of the most reliable tests which helps not only in the diagnosis but also in prognosis of the disease. The virus also causes cytopenia, neutrophilia, thrombocytopenia and coagulopathies.[7] Commonly affected parameters include platelet count, absolute lymphocyte count, neutrophil count, NLR ratio and D dimers.[8]

We carried out this study to determine hematological, coagulation and inflammatory markers in hospitalized PCR positive covid patients which can be used as a monitoring tool and give an idea about disease severity as well. Furthermore, these parameters can also give us an idea where PCR facility is not available so the suspected patients may be timely isolated, referred and managed at the desired facility.

METHODOLOGY:

This retrospective cross-sectional research was organized and managed at the Department of Pathology, in CMH Malir, a tertiary care hospital in Karachi. The study data was collected from the hospital records from 1st Aug 2021 to 31st Jan 2022. The study was conducted after approval from Hospital Ethical Review Committee (IRB no.70/2021/Trg / ERC). Sample size was calculated using WHO calculator.[8] Informed consent about the sampling and research was taken from patients or their families.

All cases which were confirmed positive after PCR testing were included in study. PCR positive patients managed outdoors were excluded from the study irrespective of their signs and symptoms.

Nasopharyngeal swabs were collected by using the recommended and standardized technique. The nasal swabs were then tested by PCR for corona virus. Further laboratory tests were performed on only those patients who turned out to be positive. Complete blood picture (Hb, WBC, platelet, neutrophil, lymphocyte), coagulation profile (PT/ APTT), D-dimer, ESR and CRP were performed.

For CBC, 3ml sample was collected in EDTA and run on haematology analyzer celtac-alpha by Nihon Kohden. For coagulation profile 2 ml venous sample was collected in Trisodium citrate bottle. PT/APTT was performed on ACL 7000 analyzer, whereas latex agglutination method detected D-Dimers with cut off value of 200ng/ml. 1 ml venous sample was taken and CRP was performed using a spectrophotometric assay. ESR was performed by westergrens methodology using automated roller 20 LC.

Following definitions were used during CBC interpretation:

Anemia : Hb <13 x g /dl in males and Hb < 11x g /dL in females.

Neutrophilia: Absolute neutrophil count > 8000/ul.

NLR ratio: The calculation of neutrophil-to-lymphocyte ratio was carried out by simple division method. In normal adults its value is 3.5.

Thrombocytopenia; Defined as platelet count of < 150 x 10^9/l.

CRP: More than 6ng/l is taken as positive.

ESR : > 15mmHg in males and > 10 mmHg in females is taken as increased.

The information was entered and interpreted using Statistical Package for Social Science (SPSS) version 23. Outcomes were framed as frequencies. To calculate P value, Chi square test was applied. A P-value of less than 0.05 was taken as significant.

RESULTS:

In this study, out of 126 admitted patients most of the presenting patients were male. The male comprised of 62 % of total while females were about 38.1 %. The age distribution is as under:

In this research, the extent of high white blood count, neutrophilia and lymphopenia is found to be 65.1%, 62.7% and 64.2% respectively. Anemia was present in 23.8 % cases. Abnormal neutrophil to lymphocyte ratio was relatively more common (62%). On the otherhand CRP and ESR, D-dimers were significantly raised which were 96.8%,92.95 and 60.3% respectively. Clotting factors PT and APTT were found to be normal in majority of patients, while inflammatory markers D-dimers and CRP were raised with a significant association P-value 0.00 and 0.028 respectively. The magnitude of raise ESR was found to be higher in most of cases i.e (92.9%).

DISCUSSION:

Anemia is one of the important clinical manifestation that has been observed with SARS-CoV-2 infection. Anemia occurs due to the changes in immune mediated system of

Table 1: Gender and age distribution of patients.

GENDER	Frequency (N=126)	Percent
Male	78	61.9
Female	48	38.1
Age	Frequency	Percent
17-35	46	36.5
36-55	41	32.5
>=56	39	31.0
Total	126	100.0

Table 2: Significance of haematological and inflammatory parameters in Covid 29 Patients

Test	Normal		Abnormal	
	Frequency	Percentage	Frequency	Percentage
D DIMERS	50	39.7	76	60.3
CRP	4	3.2	122	96.8
ESR	9	7.1	117	92.9
PT	116	92.1	10	7.9
APTT	120	95.2	06	4.8
Hb	96	76.2	30	23.8
WBC	44	35	82	65.1
NEUTROPHILS	47	37.3	79	62.7
LYMPHOCYTES	45	35	81	64.2
PLATELETS	101	80	25	19.8
NLR	48	38.1	78	62

Neutrophils to lymphocytic ratio was raised (62 %) with significant p value of 0.00

iron metabolism and homeostasis. It is quite commonly seen in elderly suffering from covid. Although it does not directly affect the mortality but it can have negative impact on the life quality of frail and elderly population. The extent of anemia in our study was found to be 23.8 %, which is comparable to a study conducted by Bellmann-Weiler et al where 24.7% of the patients were anemic and anemia was secondary to inflammation in majority of the cases.[9] However in another study, it was found to be much more common as compared our study. In this research conducted by Tao et al, it was reported to be 35.5%. This research concluded that anemia aggravates the disease and is an independent risk factor for increasing severity of disease.[10]

Center for Disease Control and Prevention (CDC) showed cases of leukopenia in (9–25%), leukocytosis in (24–30%), and lymphopenia in (63%) covid patients who reported in hospital with pneumonia.[11] In another research article by Guan et al of China which analyzed 1099 patients from 552 different hospitals and verified that 33.7%, 36.2% and 83.2%, of COVID-19 patients had leukopenia, low platelets and lymphopenias respectively. Lymphocytopenia was the most prominent finding in this research.[12] These abnormalities were more evident in severely ill patients as compared to non-severe patients. The parameters like neutrophilia, lymphopenia and raised neutrophil-to-lymphocyte ratio (NLR) have strong association with risk of acute respiratory distress syndrome (ARDS) development requiring ICU (intensive care unit) care. Similarly, some other studies demonstrated that there is association of leukocytosis, thrombocytopenia, lymphopenia and high neutrophil count with poor prognosis and critical care requirement.[12]

In our study neutrophilia and leukocytosis was found significantly increased similarly, in majority of studies conducted among acutely ill patients. However, the commonest finding was found to be neutrophilia and lymphopenia was not a significant finding in our case. One of the study by Qin et al among 138 indoor patients showed that neutrophilia was significantly higher in critically ill ICU patients (77.6%) which was comparable to our study.[13] In another research conducted by Gong et al also had similar results with (P<0.001).[14] Neutrophilia was associated with bad outcome which was also shown by Li et al.[15] Another study by Zhang et al among 82 dead COVID-19 patients also revealed that 74.3% of them had neutrophilia on admission and this increased to 100% in 24 hours before death.[16] There could be relationship of neutrophilia with the cytokine storm which is the characteristic of disease severity. One of the possibilities of high neutrophil count could be due to bacterial co-infection. One of study in China revealed that leukocytosis on admission of COVID-19 patients was associated with increased risk of death in hospital. In another research by Zhou et al[9] it is elaborated that non-survivors had more significant leukocytosis than the survivors (P<0.001).[17]

Neutrophil to lymphocyte ratio was high with significant value. Our study showed significant NLR ratio in 62 % of patients. According to a similar study conducted by Yang AP et al, some independent factors to indicate poor prognosis in COVID-19 patients include age and higher neutrophil to lymphocyte ratio.[18]

C-reactive protein is an acute phase reactant which rises in response to any inflammatory condition in body. Levels of CRP may increase with inflammation in respiratory diseases.[19] In these studies, critical covid patients in ICU revealed significantly raised CRP levels which is due to the aggressive inflammatory response described in association with severe disease and cytokine storm.[20]

We found significantly raised D-dimers levels among 60.1% patients. Coagulation parameters like prothrombin time (PT) and activated partial prothrombin time (APTT) do not reveal any significance. However, raised D-dimer levels are reported to be one of the significant prognostic factors in COVID-19 pneumonia.[21] Another research conducted in 2020 by Guo et al, revealed association of disease severity and poor outcome with raised levels of D-dimer.[22]

Most of the patients under study revealed normal platelets. Only mild decrease in platelet counts were noted in around 19.8 % of patients. Same findings were observed in a research by Chen N who reported mild thrombocytopenia in 20% of cases.[23] Similarly according to a French cohort, mild thrombocytopenia was reported in one fourth of COVID-19 admitted patients and it was reported to be an independent predictive risk factor for intensive care monitoring, ventilatory support or even death.[24]

The population under study was from similar demographic area and were the admitted patients who required monitoring and management therefore further verification is needed in different areas and in outdoor patients with mild symptoms. Outdoor patients were not included in the study.

CONCLUSION:

Our study showed that neutrophilia, leucocytosis, raised Neutrophil to lymphocyte ratio, CRP, ESR and D-dimers are important parameters among patients with COVID-19. COVID-19 disease directly affects the hematological, coagulation and inflammatory bio-markers so they should be used not only for prognosis but also to predict and intervene with effective management plan before the disease triggers to severe crisis, end organ failure or inflammatory storm.

Authors Contribution:
Faiz us Saba: Data analysis
Zunera Sajjad: Conception and design of article
Ayesha Khan: Data collection and design of article
Muhammad Iqbal: Design of article
Muhammad Faisal Faheem: Application of stats and data analysis
Nabeela Khan: Proof reading and reference writing

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