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LABORATORY SPECTRUM OF COVID-19 PATIENTS AND VARIATIONS WITH CO-MORBIDITIES: A STUDY IN TERTIARY CARE HOSPITAL OF NORTHERN INDIA

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ABSTRACT

Background: The first case of Coronavirus Disease 2019 (COVID-19) was described in Wuhan, December 2019. The virus has evolved into a pandemic over a short period of time with rapidly increasing cases and associated morbidity and mortality. Laboratory parameters like inflammatory markers and tests of fibrinolytic pathway play an important role in diagnosis and prognostication of the disease. **Methods**: It is a retrospective observational study. One hundred and fifty four hospitalized patients with diagnosis of COVID-19 over a period of 2.5 months were enrolled in the study. Laboratory parameters, presenting complaints and co-morbidities were recorded and studied. Statistical analysis was done using percentage, mean and two tailed T test. **Results**: The median age of presentation was 57.5 years. Lymphopenia was observed in 48.7% and thrombocytopenia in 24% cases. Amongst inflammatory markers, serum Ferritin was raised in 81.7%, Interleukin-6 in 76.4% and C-reactive protein in 99.2% of the patients. D-dimer analysis showed raised levels in 80.3% patients. The median age of patients with co morbidities was 61.26 years as compared to earlier presentation at 52.37 years in cases with no underlying disease (p value 0.000152). Patients with co-morbidities were associated with statistically significant higher C-reactive protein levels (p value 0.0318) and higher absolute neutrophil count (p value 0.039). Differential counts showed lower lymphocyte counts (p value 0.0329) and higher neutrophil counts (p value 0.0499) in patients with co-morbidities.

KEYWORDS: COVID, co-morbidities, D-dimer, Inflammatory markers.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) outbreak started in Wuhan, China as pneumonia of unknown origin. It developed into pandemic over a short span of time.[1] Earlier named 2019-nCoV, COVID-19 is a mutated SARS like-virus belonging to the Coronaviridae family, transmitted to humans via Bats. It has a long incubation period of two weeks and lower mortality rates which has facilitated its development into a pandemic.[2,3]

COVID-19 is a respiratory and systemic disease presenting predominantly with clinical symptoms of dry cough, malaise, dyspnea, and fever. The disease ranges from asymptomatic, severe disease to critical disease. In advanced stages of the disease it affects multiple organ systems leading to multiple organ failure.[4,5]

Early detection of infected individuals is of utmost importance to help administer early treatment and quarantine which helps in limiting spread of the virus. The World Health Organization (WHO) has advocated and approved use of Reverse transcriptase polymerase chain reaction (RT-PCR) for diagnosis of COVID-19.[6] Rapid screening tests have been developed which are cost effective, require no expensive equipment and are being used for diagnostic purpose.[7,8]

Laboratory diagnostic tests play crucial role in early and suspected disease diagnosis, disease monitoring, prognosis and follow up.[9,10] Tests done for baseline evaluation in COVID-19 patients include complete blood counts(CBC), tests of coagulation and fibrinolysis like prothrombin time (PT), activated partial thromboplastin time (aPTT) and D-dimer along with inflammatory markers like interleukin-6 (IL-6), ferritin, erythrocyte sedimentation rate (ESR) and calcitonin. In addition organ specific tests like liver function tests, renal function tests etc. are done to evaluate the effect of virus on these systems.[11]

MATERIALS AND METHOD

It is a retrospective single-center observational study. All diagnosed cases of COVID-19 admitted to hospital from 1st September to 15th November 2020 were enrolled in the study. CBC, inflammatory markers (serum ferritin, IL-6 and CRP) and D-dimer were noted from patient records. Presenting clinical complaints, co-morbidities

were also recorded. Statistical analysis was done using T test (two tail analysis), mean and percentage.

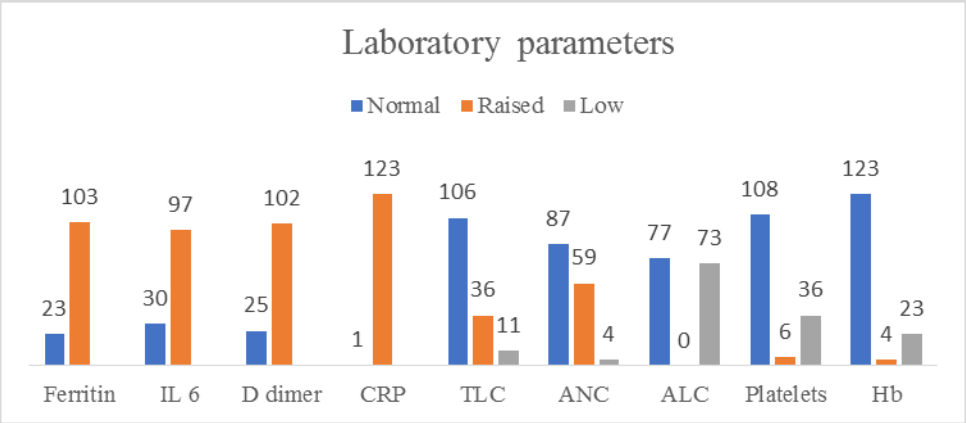
RESULTS

The mean age of presentation was 57.5 years with 105 male and 49 female patients. The mean age of presentation in male patients (56.3 years) was slightly earlier as compared to female patients (59.9 years). Majority of the cases presented with fever, difficulty in breathing and generalized weakness. Other symptoms included cough, abdominal pain, sore throat, loss of appetite, chest uneasiness, headache and loose stools. Of the 154 patients studied, eight died during the course of treatment. Seven of these patients had associated co-morbidities.

TLC was available for 153 cases and differential counts for 150 cases. One hundred and six patients presented with normal total leucocyte counts (TLC) while leukocytosis was seen in 36 patients and leucopenia in 11 patients. TLC ranged from 2200 to 26,900/cumm (average of 8755/cumm). Mean TLC was slightly higher in males (9077/cumm) as compared to females (8050/cumm).

The average absolute lymphocyte count (ALC) was 1231.2/cumm (range: 315 to 2937/cumm). Lymphopenia was seen in 73 (47.4%) patients. Neutrophilia was appreciated in 59 patients while 4 cases showed neutropenia. Absolute neutrophil count (ANC) ranged from 1221/cumm to 24210/cumm. Differential leucocyte counts (DLC) showed raised neutrophil differential (mean 74.7% neutrophils) and lower lymphocyte differential (mean 17.62% lymphocytes). Anemia was seen in 24 (15.9%) patients. Complete blood count findings are represented in table 1 and graph 1.

Three inflammatory markers were studied, namely IL-6, ferritin and CRP. D-dimer was studied for evaluation of effect of virus on fibrinolytic pathway. Serum ferritin was available for 126 cases and found to be elevated in 103 (81.7%) cases. Mean ferritin value was 287.5 ng/ml, with average of 239.4 ng/ml in females and slightly higher, 307.4ng/ml in males. Ferritin ranged from 27.28ng/ml to >1000ng/ml. D-dimer and IL6 were available for 127 cases. IL6 was raised in 97 (76.4%) cases while D dimer was raised in 102 (80.3%) cases. Mean IL6 value was 133 pg/ml (range: 2.15 pg/ml to 959.61pg/ml) while mean d dimer value was 1.4 µg/ml (range: 0.16 µg/ml to >16 µg/ml). CRP was raised in all cases but one (99.2%) with average of 61.8 mg/L. The findings are represented in and graph 1 and table 1.



Graph 1.

Table 1: Laboratory parameters (Mean Values).

	Male	Female	Overall
Cases	105	49	154
Age (years)	56.3	59.9	57.5
TLC (/cumm)	9077	8050	8755
Neutrophils (%)	76.1	71.6	74.7
ANC (/cumm)	7342.6	5937.2	6911.6
Lymphocytes (%)	16.2	20.9	73
ALC (/cumm)	1129.5	1461.1	1231.2
Hb (gm/dl)	13.7	12.6	13.4
Platelets (lakh/cumm)	2.05	2.59	2.22
Ferritin (ng/ml)	307.4	239.4	287.5
IL 6 (pg/ml)	133	133.4	133
D dimer (µg/ml)	1.3	1.6	1.4
CRP (mg/L)	61.1	63.4	61.8

Co-morbidities

Eighty eight patients presented with associated co-morbidities. Most prevalent was diabetes mellitus seen in 50 cases, followed by hypertension which was present in 47 cases. Other diseases observed included cardiac problems like coronary artery disease, atrial fibrillation, dilated cardiomyopathy (12 cases), hypothyroidism (5 cases), asthma, hepatic and renal pathology (4 cases each), seizures, cerebrovascular accident, carcinoma breast, acute pancreatitis, human immunodeficiency virus (HIV) and an old case of pulmonary tuberculosis.

Mean age of presentation of patients with co-morbidities was significantly higher at 61.26 years as compared to early presentation at 52.37 years in patients without underlying diseases. A significant correlation of co-morbidities and higher CRP values (p value 0.0318) was appreciated. IL-6 and D dimer values were higher in patients with co morbidities, however, not statistically significant. The total leucocyte count was higher in the co-morbid subgroup. In differential counts, neutrophil differential was significantly higher with mean value of 76.7% (p value 0.0499) in patients with co-morbidities. The lymphocyte differential count were lower with mean of 16% as compared to 20.1% in patients with no known underlying diseases (p value 0.0329). However, no statistically significant difference was seen in absolute lymphocyte count. A comparison of various parameters is depicted in table 2.

Table 2: Laboratory parameters comparison in patients with and without co-morbidities.

	Co-morbidities present	No known co-morbidities	P value (T test: 2 tailed)
Cases	88	66	-
TLC (/cumm)	9428	7868	0.565
Neutrophils (%)	76.7	72.3	0.0499
ANC (/cumm)	7572	6070	0.039
Platelets (lakh/cumm)	2.24	2.09	0.627
ALC (/cumm)	1225.8	1238	0.907
Lymphocytes (%)	16	20.1	0.0329
Hb (gm/dl)	13.3	13.5	0.102
Ferritin (ng/ml)	279.8	297.6	0.632
IL 6 (pg/ml)	154.6	104.9	0.177
D dimer (ug/ml)	1.62	1.11	0.138
CRP (mg/L)	69.8	50	0.0318
Age (years)	61.26	52.37	0.000152

DISCUSSION

The mean age of presentation in our study was 57.5 years which is similar to study by Chen et al. and Zhou et al. while Cao et al. and Guan et al. had earlier presentation.[12,13,14,15] Leukocytosis was observed in 23.5% cases in our study which is close to 24% and 21% in study by Chen et al. and Zhou et al. respectively.[12,14] Lymphopenia was observed in 48.7% cases which is slightly higher than studies by Chen et al., Cao et al. and Zhou et al.[12,13,14] Inflammatory markers (ferritin, IL6 and CRP) and D-dimer are increased in majority of cases. The higher rates of positivity compared to other studied can be attributed to different cut off values. The upper limit for D-dimer in study by Chen et al. was >1.5µg/ml and hence a lower positivity rate of 36%.[12] In study by Guan et al. values of >10mg/l were taken as CRP reactivity. A positivity of 60.7% was observed in COVID-19 cases.[15] Various findings and comparison with other studies is shown in tabulated form in table 3.

Table 3: Comparison of Laboratory parameters with other studies.

	Present study	Chen et al.[12]	Cao et al.[13]	Zhou et al.[14]	Guan et al.[15]
Cases	154	99	198	191	1099
Age (years)	57.5	56	50	56	47
Female (%)	31.8	32	49	38	41.9
Leukocytosis (%)	23.5	24	10.4	21	5.9
Neutrophilia (%)	39.3	38	6.2	-	-
Lymphopenia (%)	48.7	35	37.5	40	83.2
Thrombocytopenia (%)	24	12	17.6	7	36.2
Anemia (%)	15.9	51	-	15	-
D-dimer (increased) (%)	80.3	36	32	68	46.4
CRP (increased) (%)	99.2	86	78.4	-	60.7
Ferritin (increased) (%)	81.7	63	-	80	-
IL6 (increased) (%)	76.4	52	-	-	-

ALC: Lymphopenia <1100/cumm, normal: 1100-4000, Lymphocytosis >4000/cumm

ANC: Neutropenia <1500cumm, normal: 1500-7000, Neutrophilia >7000/cumm
Hb: Anemia <11.5gm/dl, Polycythemia >16.5gm/dl
Ferritin normal range: 7-140ng/ml
IL6 normal range: 0-8pg/ml
D dimer normal range: 0.0-0.5 µg/ml
CRP normal range: 0-5ml

In study by Zhou et al. comorbidities were observed in 48% cases which is lower than current study (57.1%). Unlike our study, the most common comorbidity was hypertension followed by diabetes mellitus. Others included coronary heart disease, obstructive lung disease, carcinoma, renal disorders etc.[14] Variations could be attributed to demographic differences in disease prevalence.

Present study has few limitations. All markers of inflammation like ESR, prolactin, albumin and LDH were not evaluated. Markers of hemostasis like PT and APTT were not analyzed. Laboratory values only at the time of patient admission have been studied.

RESULTS

Inflammatory markers namely ferritin, IL-6 and CRP are increased in COVID-19 patients. Elevated levels of D-dimer (80.3%) are also appreciated. CBC profile highlights lymphopenia in 48.7% patients with occasional thrombocytopenia (24% cases).

Patients with associated co-morbidities have statistically higher value of CRP, ANC, later age of presentation and lower lymphocyte differential as compared to patients with no known underlying disease.

Declaration of Interest

We declare no conflict of interests.

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