



Original Research Article

Evaluation of role of hematological parameters in patients with covid-19 infection: A study at tertiary care centre

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ABSTRACT

Background: SARS COV2 is the third known corona virus responsible for fatal respiratory illness in humans. The initial clinical features of the disease are quite often non-specific & not all suspected patients can be tested to exclude or confirm the disease. Abnormalities in the routine laboratory tests particularly haematological tests have the potential to indicate in a quick, practical & economical way, the need for a specific laboratory test for the diagnosis for SARS COV2. Besides these tests help in assisting the prognosis of the disease & in the optimization of its clinical monitoring.

Materials and Methods: The present study was prospective & observational done in the department of pathology by observing the haematological parameters of 1000 COVID positive patients admitted in the COVID hospital of a tertiary care centre. The CBC (1000 pts), coagulation profile (250 pts), ESR (100 pts) as well as peripheral smear examination (1000 pts) was done with the collected samples.

Results: 1000 samples were received for CBC which was run in 5 part Horiba analyzer & significantly higher values were found in TLC, Neutrophil count as well as N:L ratio, while lymphocyte values were significantly decreased. Thrombocytopenia was present in a significant number of patients & so were high ESR values. Coagulation profile was significantly deranged & so were the peripheral smear findings.

Conclusion: Hematological abnormalities in COVID 19 are related with disease progression, severity & mortality.

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1. Introduction

Coronavirus disease causing severe acute respiratory syndrome has rapidly evolved into a global pandemic effecting more than 100 million individuals worldwide.¹

SARS COV2 is the third known corona virus responsible for fatal respiratory illness in humans. The initial clinical features of the disease are quite often non-specific & not all suspected patients can be tested to exclude or confirm the disease. Abnormalities in the routine laboratory tests particularly hematological tests have the potential to indicate in a quick, practical & economical way, the need

for a specific laboratory test for the diagnosis for SARS COV2. Besides these tests help in assisting the prognosis of the disease & in the optimization of its clinical monitoring.

Patient suffering from COVID-19 shows alterations of many hematological parameters like Total WBC count, Hemoglobin, Neutrophil count, Lymphocyte count, NLR (neutrophil lymphocyte ratio) & Platelet count, Coagulation profile, ESR and Peripheral smear examination. Platelet count is a simple and effortlessly available hematological parameter, which is independently associated with disease severity and risk of mortality in the intensive care unit (ICU). Coagulopathies like disseminated intravascular coagulation, sepsis-induced coagulopathy (SIC), local

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microthrombi, venous thromboembolism (VTE), arterial thrombotic complications, and thrombo-inflammation have been associated with COVID-19.²

This study was carried out to observe the changes of various hematological parameters in patients with SARS COV2 infection & to determine the role of parameters at a tertiary care centre.

2. Aims & Objectives

1. To evaluate the role of hematological parameters in SARS COV2 positive patients.
2. To evaluate coagulation profile in SARS COV2 positive patients.

3. Materials and Methods

3.1. Type of study

Prospective.

3.2. Number of patients

COVID positive patients.

3.3. Materials

1. EDTA & Citrate Vacuette containing Venous whole blood & serum.
2. PPE Kit.
3. Appropriate biohazard waste container & disinfectant.

Full aseptic precautions were taken.

3.4. Methods

1. For CBC: 5 part Horiba analyzer machine was used (fully automated).

For peripheral smear examination routine smear preparation followed by staining by leishman stain & examination under oil immersion microscope was done.

For PT/APTT/D dimer- STAGO Machine was used (fully automated)

3.5. Report entry

1. Entry of test report in separate reporting register was done.

Reports were stored in COVID-19 reporting box separately.

3.6. Discard policy

There was a separate yellow container with yellow discard bag for COVID-19 sample Vacuette, gloves & masks. Outer bag was labelled as COVID-19 biomedical waste & segregated & discarded according to the BMW disposal policy of the government of India.

3.7. Inclusion criteria

1. All laboratory confirmed case (by RT-PCR/Rapid test).
2. Admitted positive cases with on-going treatment.

3.8. Exclusion criteria

Suspected cases with symptoms of URTI but negative for test result OR test not done.

4. Results

Total of 1000 patients were studied who had tested positive for SARS COV2 by either Rapid antigen test or RT PCR test. Various hematological parameters were studied after doing a CBC examination. Similarly coagulation profile was studied. ESR as well as peripheral smears of the patients was also studied & following results were obtained.

Table 1: Age distribution in COVID 19 patients (n-1000).

Age	No. of patients	Percentage (%)
0-10	06	0.6%
10-20	08	0.8%
20-30	63	6.3%
30-40	98	9.8%
40-50	156	15.6%
>50	669	66.9%
Total	1000	100%

From above table it is observed that majority of the patients (66.9%) who required hospitalization were above the age of 50 years followed by 15.6% in the age group of 40 to 50 years. All other age group persons were affected less commonly. Table 1

Table 2: Gender distribution in COVID 19 positive patients (n-1000)

Gender	No. of patients	Percentage (%)
Male	610	61%
Female	390	39%
Total	1000	100%

The above table shows that male patients were more commonly affected (61%) than females (39%). Table 2

Table 3: Common Complaints encountered in COVID 19 positive patients (n= 1000)

S.No.	Chief Complaints	No. of patients	Percentage %
1	Cough	210	21%
2	Weakness	722	72.2%
3	Fever	419	41.9%
4	Breathlessness	196	19.6%
5	Loss of taste/smell	163	16.3%

Many patients had more than one complains. Most common complaints being weakness and fever followed by cough, breathlessness and loss of taste/smell. Table 3

Table 4: Haemoglobin values in COVID 19 positive patients (n=1000)

Age group	HB <10 gm/dL	10-12 gm/dL	>12 gm/dL
0-10	00 (0%)	00 (0%)	06(0.6%)
10-20	00 (0%)	01 (0.1%)	07(0.7%)
20-30	11 (1.1%)	24(2.4%)	28(2.8%)
30-40	18 (1.8%)	43(4.3%)	37(3.7%)
40-50	19(1.9%)	42(4.2%)	95(9.5%)
>50	39(3.9%)	218(21.8)	412(41.2%)
Total	87(8.7%)	328(32.8%)	585(58.5%)

From Table 4 it is seen that majority of patients (58.5%) had hemoglobin in the normal range (>12gm/dl) while 8.7% patients had decreased haemoglobin of <10 gm/dl the others (32.8%) had haemoglobin values in between the above two (10-12gm/dl).

Table 5: Total Count in COVID 19 positive patients (n=1000)

Age group	<4000	4000-11,000	>11,000
0-10	00(0%)	00(0%)	06(0.6%)
10-20	00(0%)	01(0.1%)	07(0.7%)
20-30	03(0.3%)	31(3.1%)	29(2.9%)
30-40	05(0.5%)	52(5.2%)	41(4.1%)
40-50	06(0.6%)	89(8.9%)	61(6.1%)
>50	08(0.8%)	284(28.4%)	377(37.7%)
Total	22 (2.2%)	457 (45.7%)	521 (52.1%)

From above table it is observed that majority of the patients (52.1%) had leucocytosis in the range of >11,000 cells/cumm while 45.7% had normal leucocyte count in the range of 4000-11,000 cells/cumm and 2.2% had leucopenia total count being <4000 cells/cumm. Table 5

Table 6: N:L Ratio (Neutrophil: Lymphocyte ratio) IN COVID 19 positive patients (n=1000)

Age group	<3	>3	Total
0-10	3(0.3%)	3(0.3%)	06
10-20	3(0.3%)	5(0.5%)	08
20-30	18(1.8%)	45(4.5%)	63
30-40	51(5.1%)	47(4.7%)	98
40-50	62(6.2%)	94(9.4%)	156
>50	221(22.1%)	448(44.8%)	669
Total	358(35.8%)	642(64.2%)	1000

Out of total 1000 patients 64.2% (642 patients) had NLR of >3 while remaining 35.8% (358 patients) had NLR of <3. Patients having higher NLR had poor general outcome and required either ventilator support or died due to the disease. (Note: patients showing ~90% neutrophilia or ~3-4% lymphopenia showed poor prognosis). Table 6

Table 7: Platelet count in COVID 19 positive patients (n=1000)

Type	Range of platelet count/ml	No of patients	Percentage (%)
Normal	150000 to 450000	350	35%
Mild thrombocytopenia	100000 to 150000	335	33.5%
Moderate thrombocytopenia	50000 to 99000	202	20.2%
Severe thrombocytopenia	<50000	113	11.3%
Total		1000	100%

Table 7 shows that 33.5 % patients had mild thrombocytopenia, 20.2 % had moderate While only 11.3 % had severe thrombocytopenia necessitating vigorous treatment. Overall 65 % patients showed thrombocytopenia while 35 % had normal platelet count.

Table 8: ESR values in COVID 19 positive patients (n=100)

ESR in mm at 1 st hour	No. of Patients	Percentage
<20	12	12%
20-40	34	34%
>40	53	53%
>100	01	01%
Total	100	100%

From the Table 8 it is observed that majority of patient (53%) had ESR >40 mm/hour, while 34% of patient had ESR in range of 20-40 mm/hour and 12% had ESR <20 mm/hour.

Table 9: Peripheral smear in covid 19 positive patients (n=1000).

PS Abnormalities	No. of Patients
PS with Normal Finding	336(33.6%)
Leucopenia	22(2.2%)
Lymphopenia	642(64.2%)
Neutrophilia	642(64.2%)

Above Table 9 that majority of patients had neutrophilia (64.2%) with lymphopenia.

4.1. Coagulation profile in covid 19

Table 10: Prothrombin time (P.T) in COVID 19 positive patients (n=250)

Prothrombin time (Seconds)	No. of patients
<11	00
11-16	127(50.8%)
>16	123(49.2%)
Total	250

From Table 10 it is observed that 50.8% patient had normal value of PT in range of 11-16 sec, while 49.2 patient had more value of PT (>16 sec).

Table 11: APTT in COVID 19 positive patients (n=250)

APTT (Seconds)	No. of patients
<35	47(18.8%)
35-45	120(48%)
>45	83(33.2%)
Total	250

From the Table 11 it is observed that majority of patient (48%) had normal value of APTT in range of 35-45 sec, while 18.8% of patient had Low value of APTT <35 sec and 33.2% patient had high value of APTT >45.

Table 12: INR values in COVID19 positive patients.(n=250)

<1	60
1-1.5	117
>1.5	73
Total	250

From the Table 12 it is observed that majority of patient (117 out of 250) had INR ratio in range of 1-1.5, while 60 patient out of 250 patient had INR ratio <1 and 73 patient out of 250 patient had INR ratio >1.5.

Table 13: D-Dimer in COVID 19 positive patients (n=200)

D- Dimer test result	No. of patients
Positive	77(38.5%)
Negative	123(61.5%)
Total	200

From the Table 13 it is observed that 61.5% patient had Negative result of D-DIMER, while 38.5% patient had Positive result of D-DIMER.

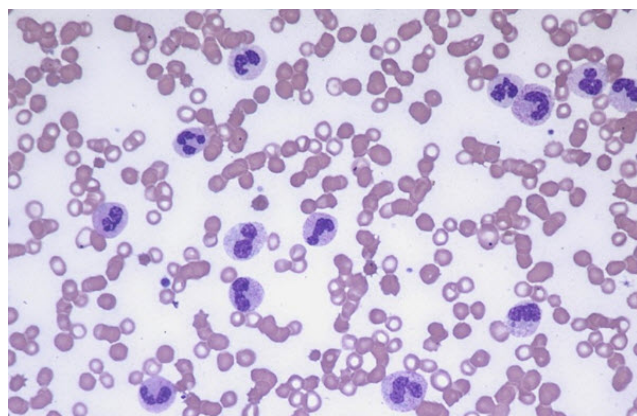


Fig. 1: Peripheral smear showing Neutrophilia (leishman stain)

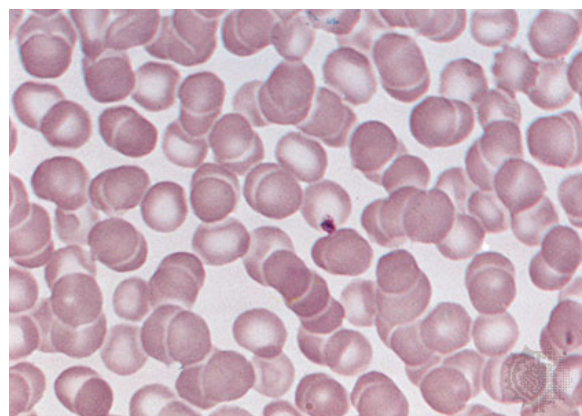


Fig. 2: Peripheral smear showing lymphopenia (leishman stain)

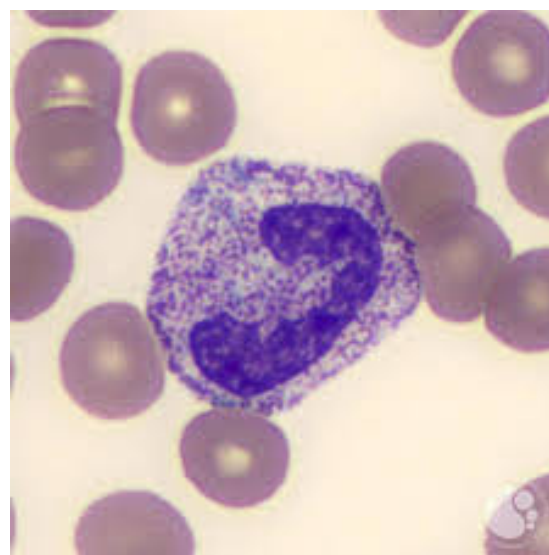


Fig. 3: Peripheral smear showing toxic granulation.



Fig. 4: Peripheral smear showing C-shaped neutrophil.

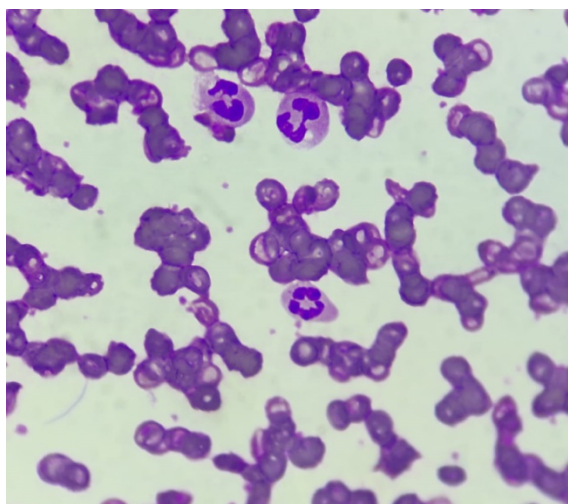


Fig. 5: Peripheral smear showing ring neutrophil.

5. Discussion

SARS COV2 shows more positivity in the middle & older age groups as compared to younger population. Males are affected more than females owing to the outdoor work of most of the males & hence more public exposure. Most common presenting complaint was fever & weakness followed by breathlessness especially in patients having co-morbidities or those who ignored their symptoms initially thinking it to be simple common cold. A patient with various co-morbidities almost always required hospitalization with oxygen support.

As for hematological parameters, hemoglobin (Hb) was in near normal range in most of the patients, while total leucocyte count (TLC) was high in initial phase followed by a dip in subsequent workup suggesting improvement. In patients with normal range or low TLC home quarantine with adequate fluid & vitamin support was the adequate treatment in most of the cases thus reducing the load on health care system & resources. In patients with persistently high total leucocyte count, severe disease was suggested requiring vigorous treatment & thereby hospitalization. In differential leucocyte count (DLC) most common spectrum was severe neutrophilia with lymphopenia. About 64 % patients had N: L ratio of > 3 on admission suggesting a grave prognosis. Erythrocyte sedimentation rate (ESR) was high in $> 50\%$ patients in the range of > 40 mm/hr. suggesting the inflammatory nature of the disease. Thrombocytopenia was present in about 65 % of patients varying from mild, moderate to severe levels. Severe thrombocytopenia was associated with grave prognosis.

In peripheral smear examination most of the cases showed leucocytosis with neutrophilia along with toxic granulations, ring shaped neutrophils & C shaped neutrophils (Figures 1, 2, 3, 4 and 5)

Coagulation profile needs special mention because SARS COV2 virus causes D.I.C like symptoms in severe cases. In our study close to 50% patients showed a higher Prothrombin Time (P.T) value of >16 seconds, APTT was higher than 35 seconds in around 35 % patients While an INR of significance could be seen in close to 35% patients. Qualitative D Dimer positivity was seen in around 40% suggesting that significant amount of fibrin degradation product & D.I.C was present in circulation of patient thus requiring appropriate thrombolytic therapy.

Poor prognostic parameters such as N:L ratio of > 3 , increased ESR, decreased platelets increased PT, APTT, INR values as well as persistently high D Dimer levels were seen in patients with severe disease requiring hospitalization with intensive therapy, oxygen therapy with Bipap and/or ventilator support.

Comparison with other authors studies showed similar results as our study.

Sadia Taj et al³ demonstrated that Leukocytosis, neutrophilia and increased neutrophil to lymphocyte ratio, which might be due to inflammatory response, have a significant association with the disease severity. Neutrophil to lymphocyte ratio was highest in patients with critical disease. Liao D et al.⁴ also found elevated neutrophil to lymphocyte ratio as a useful predictor for severity and mortality of SARS-CoV-2 infection

Lymphopenia was present in 83.2% of patients on admission according to study by Guan et al⁵ & 85% by Huang et al.⁶ Huang et al and Wang et al⁷ highlighted an association between lymphopenia and need of ICU care, whereas Wu et al.⁸ showed an association between lymphopenia and acute respiratory distress syndrome (ARDS) development

The association of NLR with severity of covid-19 disease was also concurred by a study of Yang AP et al,⁹ who concluded that high neutrophil to lymphocyte ratio and age are the independent factors for indicating poor clinical outcome of covid-19 patients

Thrombocytopenia was defined as a platelet count of less than $150\,000/\text{mm}^3$ & was further categorised as mild, moderate & severe. A meta-analysis of nine studies has suggested that thrombocytopenia is significantly associated with the severity of the COVID-19 disease. Severe cases presented thrombocytopenia more frequently (57.7%) (Guan et al). In a study by Huang et al. 8% of patients needing ICU care presented with low platelet counts.

The most common pattern of coagulopathy observed in patients hospitalized with COVID-19 is characterized by elevations in fibrinogen and D-dimer levels, and mild prolongation of PT/aPTT. This correlates with a parallel rise in markers of inflammation (e.g. CRP). Unlike the pattern seen in classic DIC from bacterial sepsis or trauma, prolongation of the aPTT and/or PT is minimal, thrombocytopenia is mild (platelet count $\sim 100 \times 10^9/\text{L}$),

and lab results supporting microangiopathy are infrequent. Rarely patients with severe COVID-19 infection and multiorgan failure progress to coagulopathy meeting criteria for overt DIC.¹⁰

Hemoglobin, Mean Corpuscular Volume (MCV) and haematocrit (PCV) of the COVID-19 patients showed no significant association with the severity of disease in our study.

6. Conclusion

Hematological abnormalities in COVID 19 are related with disease progression, severity & mortality. Neutrophilia, Lymphopenia, thrombocytopenia, abnormal coagulation profile & sepsis leading to disseminated intravascular coagulation (DIC) is very well documented in COVID 19 patients.

Other tests such as ferritin, Pro-calcitonin & IL6 have also been studied to have a promising role in depicting the disease progression & hence the vigorous therapy but is not available at our centre.

COVID-19 disease has prominent manifestations from the hematopoietic system and is often associated with a major blood hypercoagulability. Careful evaluation of laboratory indices at baseline and during the disease course can assist clinicians in formulating a tailored treatment approach and promptly provide intensive care to those who are in greater need. Preventive measures for thrombo-prophylaxis and early identification of potentially lethal complications including DIC in order to effectively intervene will improve patient outcomes, and will probably reduce the death rate overall and among infected patients without significant comorbidities. Continuous vigilance is necessary and urgent studies have to be planned to define whether optimal anticoagulation regimen with or without adjunctive antithrombotic therapies may be helpful in patients with COVID-19.

This study is useful for evaluation of prognostic parameters & therapeutic responses & therefore efficiently manage the medical resources which can thereby decrease the overall mortality & morbidity significantly

7. Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

8. Source of Funding

None.

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