

Original Paper

Identifying Haematological Changes in Asymptomatic COVID-19 patients and its impact on channelizing laboratory resources

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ABSTRACT:

The unresolved COVID pandemic is an enigma to the doctors worldwide as the virus has been frequently changing its strains and clinical presentation. This has led to a heavy burden on the hospital and laboratory resources and a need to channelize the resources towards early diagnosis and treatment was strongly felt after the second wave of the pandemic. So at the start of the third wave of the pandemic in India (Jan- Feb 2022) we started closely following up the CBC findings of the COVID positive patients and were slowly able to accurately raise suspicion of COVID in patients presenting with mild symptoms or no symptoms. This helped us in early detection and lesser load on hospital resources. 320 COVID positive patients were analysed against 300 COVID negative controls and a chi square test was run. Hematological findings in early asymptomatic cases of covid display a slightly different pattern from hospitalised patients. As most of the data available is from hospitalised patients, this study could help in identifying patients with a higher probability of Covid positivity. Monocytosis was observed as an early sign in asymptomatic patients. Leucopenia, Anemia, and eosinopenia were not observed in a significant population of patients indicating that these signs probably evolve later during the course of disease.

Keywords: COVID-19, CBC, early detection, Monocytosis

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INTRODUCTION

Emerging in the city of Wuhan in Hubei province of China towards the end of 2019, corona virus has led to over 500 million cases and over 6.3 million deaths worldwide¹. The unresolved pandemic is still an

enigma to the doctors worldwide as the virus has been frequently changing its strains and clinical presentation. Though vaccinations have helped a lot in decreasing the severity of the disease, molecular detection of the virus still remains the mainstay in diagnosis. Spreading through direct person to person

contact, mainly through respiratory secretions, the virus was also found in non-respiratory specimens including stool, blood, ocular secretions and semen. Sars-Cov-2 has been detected in stool samples even after viral RNA could no longer be detected in upper respiratory sample. Scattered reports of clusters in residential buildings and dense urban community with poor sanitation suggested possibility of transmission through aerosolization of virus in sewage damage.^{1,2}

Acute respiratory distress and subsequent respiratory failure are the leading cause of death in COVID-19-positive patients. The clinical manifestations of novel COVID-19 vary from asymptomatic to acute respiratory distress, depending on virus route of entry, virus load, host immunity, and comorbidity human. Respiratory and gastrointestinal infection represent the bulk of the COVID-19-positive patient presentation, yet, asymptomatic/presymptomatic infection is estimated to be 40% of all cases.¹³ Many extrapulmonary neurological, dermatological, and cardiovascular manifestations have been frequently reported independent of respiratory infection.^{1,2}

Neutrophils are believed to have a major role in the patho-physiology of the disease. Severe Covid-19 was marked by abundance in nasopharyngeal epithelium and later in the distal parts of the lung³.

AIM OF THE STUDY

The entire world grappled with catastrophic human loss during the first and second COVID waves. Limited availability of RTPCR testing had a minimal impact in improving the situation. At Precision Diagnostics, we closely followed the CBC pattern of COVID positive patients from the start of the third wave as it is the most consistent test available in patients reporting with short history of fever. The majority of early published laboratory findings of non-severe COVID-19 infection are collected from hospital admitted patients at a single time point which limits our understanding of the dynamic haematological changes during the course of the disease. Asymptomatic patients constitute at least 20-40% of the cases. Hence the emphasis of current study is to identify such patients even before molecular testing can be undertaken or completed.

Identifying haematological changes during early testing can help in raising suspicion of Covid in asymptomatic or mildly symptomatic patients. Careful evaluation of early indicators in COVID positive,

Details of the same are mentioned in table 1 and figure 1 below

asymptomatic or mildly symptomatic patients can help in studying identifying possible cases of Covid and early isolation before the molecular testing can be completed.

MATERIALS AND METHODS

CBC findings of 320 asymptomatic / mildly symptomatic patients who tested positive for COVID at Precision Diagnostics, Ahmedabad, Gujarat, India were retrospectively studied taking into account, Hemoglobin, RBC indices, total and differential WBC counts and platelet counts and were analysed against 300 non-covid controls. All these samples were run on Mindray BC-5130 system. The data obtained was analysed using IBM SPSS software. A Chi square test was done to obtain p value and Odds ratio.

OBSERVATIONS

CBC indices of 320 Covid positive patients were studied for specific patterns in asymptomatic or mildly symptomatic covid patients. The findings were compared with 300 covid negative patients presenting to lab. The following observations were made.

No major changes in haemoglobin were noted in the Covid positive patients. In our group 8/320 (2.5%) had haemoglobin in the range of 5-9 gm/dl, 61 (19%) had haemoglobin in range of 9.1-12gm/dl while the remaining 251 (78.5%) had haemoglobin > 12.1 gm/dl. Red cell indices did not show any specific changes.

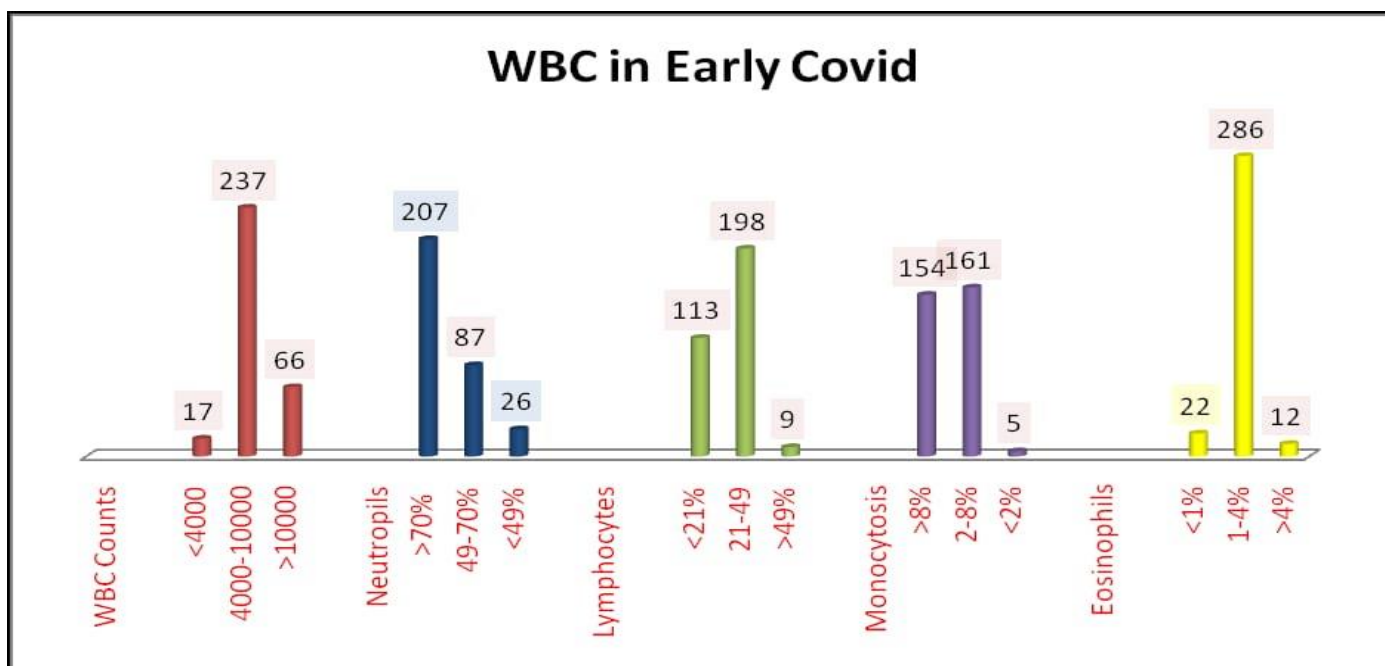
Thrombocytopenia was found in only 44/320 patients (13.75%). Leucocyte counts were in the normal range (4000-10000/ cu.mm) in 237/320 patients (74.1%), 66 patients (20.6 %) had leucocytosis while only 17 (5.3%) had leucopenia. Relative Neutrophilia was observed in 207 patients (64.7%). Lymphopenia was observed in 113 patients (35.3%). Monocytosis was observed in a total of 154 patients (48.2%) . Out of these, 126 had monocytosis with normal NLR while only 28 patients had monocytosis with increased NLR. NLR (Neutrophil to lymphocyte ratio was increased (>3.5) in 139/320 cases (43.43%) On analysing this data against the controls a significant association was noted with monocytosis, relative neutrophilia, leucopenia, thrombocytopenia and neutrophil lymphocyte ratio (p value <0.05) and Odd's ratio >1. No association was noted with anemia, leucopenia and eosinopenia suggesting possibility of evolution in the later course of the disease in severe cases.

Table 1

CBC FINDINGS IN ASYMPTOMATIC/ MILDLY SYMPTOMATIC CASES OF COVID 19

	cases (n=320)		control (n= 300)		p value	OR	95% CI
	n	%	n	%			
Hemoglobin							
<5g/dl	3	0	0	0	0.2578	5.5527	0.2851 to 108.1310
5-9g/dl	8	2.50%	12	4%	0.1714	0.5286	0.2120 to 1.3180
9.1-12g/dl	61	19%	89	29.60%	0.0014	0.514	0.3734 to 0.7908
12.1 g/dl	251	78.50%	199	66.30%	R	R	R
WBC Counts							
<4000	17	5.30%	12	4%	0.2471	1.561	0.7327 TO 3.3474
4000-10000	237	74.10%	262	87.30%	R	R	R
>10000	66	20.60%	26	8.70%	<0.0001	2.8062	1.7249 to 4.5654
Neutropils							
>70%	207	64.69%	6	2	<0.0001	78.1207	33.3903 to 182.77
49-70%	87	27.19%	197	65.6	R	R	R
<49%	26	8.12%	97	32.4	0.0508	0.6069	0.37678-1.0017
Lymphocytes							
<21%	113	35.30%	8	2.7	<0.0001	19.5467	9.3259-40.9692
21-49	198	61.80%	274	91.3	R	R	R
>49%	9	2.80%	18	6	0.3792	6919	0.3045-1.5722
Monocytes							
>8%	154	48.12%	39	13	<0.0001	6.2542	4.1799-9.3578
2-8%	161	50.30%	255	85	R	R	R
<2%	5	1.56%	6	2	0.6512	1.3199	0.3963-4.3959
Eosinophils							
<1%	22	6.87%	18	6	0.7489	1.111	0.5829-2.1181
1-4%	286	89.37%	260	86.6	R	R	R
>4%	12	3.75%	22	7.3	0.0573	0.4959	0.2406-1.0220
platelet count							
<50000	8	2.50%	3	1	0.1376	2.7536	0.732-10.4869
50000-100000	11	3.44%	1	0.33	0.0204	11.3587	1.4567-88-5722
100000-150000	25	7.81%	11	3.67	0.0217	2.3468	1.1330 to 4.8612
>150000	276	86.25%	285	95	R	R	R
Neutrophil / Lymphocyte ratio							
>3.15	47	14.69	16	5.33	0.0002	3.0559	1.692-5.519
0-3.15	273	85.31	284	94.7	R	R	R

Figure 1



Most of these findings were in accordance with the previous reports on Hematological changes in Covid except the appearance of monocytosis. This was probably an early indicator of the disease found in mildly symptomatic cases.

Based on these findings, we were able to raise suspicion of Covid and suggest the need for an RTPCR test.

DISCUSSION

Most of the data available so far for reference is from hospitalised patients. So we felt the need to carefully study simple basic tests which could raise suspicion of covid and hence a better channelization of resources towards testing could be done.

The following facts associated with COVID- 19 were available to date:

Leucopenia and lymphopenia : the normal or reduced leucocyte count is frequent. Studies which have looked into the WBC changes in hospitalized COVID-19 patients with none severe symptoms reported a total WBC count range of $3.1-7.6 \times 10^9/L$ with a mean of $4.3-5.7 \times 10^9/L$ ^{3,4}. Lymphocytopenia was reported in 80.4% of none sever patients; however, mean lymphocyte counts was more $1.0 \times 10^9/L$ in most of the cases. Leucopenia reported in 28.1% of this category with mean neutrophil count reported by different studies to be $0.4-6.6 \times 10^9/L$. This presents a prognostic value; there is likely an association between lymphopenia and the need for the Intensive Care Unit

(ICU) care, acute respiratory distress syndrome and longer stay at the hospital. Increased neutrophils has also been associated with the increased risk of death^{3,4}. Platelet counts: some studies have suggested that thrombocytopenia is associated with the severity of the disease while others that patients with significantly elevated platelets had longer average hospitalization stays.^{5,7} Several studies have shown neutrophil-to-lymphocyte ratio (NLR) as an independent risk factor for mortality in severely ill patients with COVID-19 with a cut-off value varied between 3.0 and 13^{3,8,9}. Hypercoagulability and elevated D-dimers: blood hypercoagulability is common among hospitalized COVID- 19 patients and venous thromboembolic events seem to be more frequent in the critically ill patients admitted to the ICU with this syndrome.^{6,7} The correlation between the hypercoagulability and a worse outcome may be justified by the progression to disseminated intravascular dissemination (DIC) and/or the microvascular thrombosis that leads to hypoxemic respiratory failure^{5,6}.

Comparing to the available data from hospitalised patients, COVID positive OPD patients had relative neutrophilia and monocytosis with a significant p value and high Odd's ratio suggesting a strong disease causing association with the disease. Leucopenia, anemia and eosinopenia were observed in a very small fraction of patients probably indicating their evolution in the later phases of the disease. Neutrophil to

lymphocyte was also altered only in a very small proportion of patients indicating its relationship to severity of the disease. A statistically significant Chi square test with p value <0.05) and Odd's ratio >1, suggested significant association with monocytosis, relative neutrophilia, lymphopenia, thrombocytopenia and neutrophil lymphocyte ratio. As opposed to the existing reports from hospitalised patients, no association was noted with anemia, leucopenia and eosinopenia suggesting possibility of evolution in the later course of the disease in severe cases

CONCLUSIONS

Hematological findings in early asymptomatic cases of covid display a slightly different pattern from hospitalised patients. As most of the data available is from hospitalised patients, this study could help in identifying patients with a higher probability of Covid positivity. Monocytosis was observed as an early sign in asymptomatic patients. Leucopenia, Anemia, and eosinopenia were not observed in a significant population of patients indicating that these signs probably evolve later during the course of disease.

As against the available data from hospitalised patients which was more useful in prognostication, data from asymptomatic or mildly symptomatic OPD patients with short history of fever and no definitive respiratory symptoms could help in raising suspicion and advising molecular testing for Covid thereby helping channelizing laboratory testing resources particularly RTPCR, early intervention wherever needed and also chances of missing out false negatives in cases of early covid testing.

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