

Original Article

A Study on Correlation of Pattern of Fever in Covid 19 Positive Patients with Correlation to Biochemical Parameters

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ABSTRACT

Introduction: The novel coronavirus, SARS-CoV-2 presented with a wide array of clinical, inflammatory and radiological manifestations. Currently, a very few data is available about the relationship in between pattern of fever and biochemical parameters in patients affected by COVID-19. Our objective is to find out the clinical and inflammatory status of COVID-19 patients and whether there is a relationship in between pattern of fever and biochemical parameters of severe acute respiratory syndrome coronavirus disease 2.

Methodology: A retrospective study conducted on 60 COVID-19 positive patients, who were clinically/ radiologically evaluated and screened for inflammatory markers.

Result: 39 men and 21 women had Fever and elevated inflammatory markers like CRP, D-dimer, ferritin, ESR. Altered neutrophil lymphocyte ratio was also found. Patients with moderate and severe grade fever had more significant rise in CRP (60%), D-dimer (50%). patients with mild and moderate fever had more rise of ferritin (65%). ESR and NLR were not significantly increased. Patients with intermittent fever had high rise in CRP (80%), D-dimer (75%), and ferritin (72%). Again, ESR was not significantly raised. NLR was moderately raised in patients with continuous fever (66%). Sub acute and chronic rise of temperature shows more significant rise in CRP (60%), D-dimer (82%), ferritin (80%), NLR and ESR.

Conclusion: Our study results shows that fever pattern in COVID-19 infection correlates with the inflammatory biochemical markers. Our study might be of help regarding early diagnosis of severity and timely intervention of COVID-19 infected patients to prevent morbidity and mortality.

Keywords: Fever in COVID-19, Type of fever, Duration of fever, Pattern of fever, Biochemical inflammatory markers

INTRODUCTION

Since the end of 2019, world has been witnessing the emergence of the coronavirus disease 2019 (COVID-19) outbreak and pandemic caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Till now more than 17 million cases have been confirmed worldwide.² Since the very beginning of the COVID-19 outbreak, the new disease has demonstrated varying degrees of severity with clinical characteristics.³ Direct viral effect and immune mechanisms are two major pathogenesis.⁴ The disease which was declared as a pandemic in early March 2020, is characterized by fever, dry cough, myalgia and extreme fatigue, may range from asymptomatic or with minimal flu-like constitutional symptoms to an acute respiratory distress syndrome (ARDS) with respiratory failure requiring mechanical ventilation, and at times accompanied by hyperferritinemia and multiple organ involvement including hematological, gastrointestinal, neurological and cardiovascular complications leading to death.^{5,6,7,8} among them ,a significant percentage i.e. almost 78 % of patients presented with fever.⁹ COVID -19 infection confirmation depends upon RT-PCR assay. But it takes days for the result and sensitivity ranges from 42 -83%¹⁰.so the role of biochemical parameters and HRCT thorax in suspected patients with low oxygen saturation or clinical distress is very important and continuously evolving. In this study we present the association between type, duration and severity of fever and biochemical inflammatory markers.^{11, 12, 13}

METHODS

Between February 2021 to April 2021, we enrolled 60 adult patients (39 men and 21 women), admitted to our tertiary care centre. All the patients were positive for SARS-CoV-2 as the presence of infection was confirmed by real-time reverse-transcriptase-polymerase chain reaction (RT - PCR) on nasopharyngeal swab samples. All the samples analyzed in this study were collected after hospital admission and after taking proper consent. Any patient who is pregnant or aged below 12 years or having any surgical emergency was excluded from the study. After meeting inclusion and exclusion criteria and taking proper consent detailed history taking and clinical examination was done. Patients were divided based on severity, duration and pattern of fever. Biochemical parameters were obtained from blood samples. This study was approved by the ethics committee of this institution.

RESULTS

Demographics and baseline of 60 hospitalized patients with COVID-19 are that the age of the patients considered in this study was between 23 and 74 years. Patients included 39 men (65%) and 21 women (35%).

Table 1: Association of severity with CRP, D-dimer, Ferritin, NLR and ESR

Biochemical markers	Temp 38-39 (%)	Temp 39-40 (%)	Temp >40 (%)
CRP			
< 10	4 (17.4)	1 (3.8)	1 (9.1)
10 - 50	13 (56.5)	10 (38.5)	8 (72.7)
> 50	6 (26.1)	15 (57.7)	2 (18.2)
D - dimer			
< 0.5	3 (13.04)	2 (7.6)	5 (45.5)
0.5 - 0.9	7 (30.4)	7 (26.9)	2 (18.2)
> 0.9	13 (56.5)	17 (65.5)	4 (36.3)
Ferritin			
< 300	4 (17.4)	6 (23.1)	3 (27.3)
> 300	19 (82.6)	20 (76.9)	8 (72.7)
NLR			
< 9	19 (82.6)	12 (46.2)	3 (27.3)
9-18	4 (17.4)	14 (53.8)	3 (27.3)
>18	0	0	5 (45.4)
ESR			
< 40	17 (73.9)	16 (61.5)	9 (81.8)
> 40	6 (26.1)	10 (38.5)	2 (18.2)

Table 2: Association of pattern with CRP, D-dimer, ferritin, NLR, ESR

Biochemical markers	Pattern	
	Intermittent (%)	continuous (%)
CRP		
< 10	6 (11.1)	0
10 - 50	26 (48.1)	5 (89)
> 50	22 (40.8)	1 (11)
D-dimer		
<0.5	9 (16.7)	2 (33.3)
0.5- 0.9	15 (27.8)	1 (16.7)
>0.9	30 (55.7)	3 (50)
Ferritin		
<300	11 (20.4)	2 (33.3)
>300	43 (79.6)	4 (66.7)
NLR		
<9	30 (55.5)	2 (33.3)
9-18	19 (35.2)	4 (66.7)
>18	5 (9.3)	0
ESR		
<40	37 (68.5)	5 (83.3)
>40	17 (31.5)	1 (16.7)

Like all viral infections, the presence of COVID-19 disease leads to an inflammatory response. Inflammatory status of the 60 patients with COVID-19 was evaluated considering the common diagnostic inflammatory markers: neutrophil lymphocyte ratio, ESR, CRP, D-dimer, ferritin.

Based on severity, fever has been classified as mild (38° - 39°c), moderate (39°-40° c) and severe (>40°c).

So, patients with moderate and high-grade fever had more increase in CRP than those with mild fever. Patients with moderate and high-grade fever had more increase in D-dimer than those with mild fever. Patients with moderate and high-grade fever had more increase in ferritin than those with mild fever. Patients with moderate and high-grade fever had less increase in NLR than those with mild fever.

Table 3: Association of duration with CRP, D-dimer, ferritin, NLR, ESR

Biochemical markers	Duration (days)		
	1-7 (%)	8-14 (%)	>14 (%)
CRP			
< 10	1 (5)	4 (11)	0
10 - 50	5 (25)	14 (41)	2 (40)
> 50	3 (15)	17 (48)	3 (60)
D-dimer			
<0.5	7 (35)	4 (11)	0
0.5- 0.9	5 (25)	9 (27)	0
>0.9	8 (40)	22 (62)	5 (100)
Ferritin			
<300	7 (35)	5 (15)	0
>300	13 (65)	30 (85)	5 (100)
NLR			
<9	8 (40)	15 (43)	2 (40)
9-18	10 (50)	19 (54)	1 (20)
>18	2 (10)	1 (3)	2 (40)
ESR			
<40	7 (35)	5 (15)	0
>40	13 (65)	30 (85)	5 (100)

Patients with moderate and high-grade fever had less increase in ESR than those with mild fever.

Based on pattern, fever has been classified as intermittent (temperature touches baseline daily) and continuous (temperature never touches baseline).

So, patients with intermittent fever had more increase in CRP than those with continuous fever. Patients with intermittent fever had more increase in D-dimer than those with continuous fever. Patients with intermittent fever had more increase in ferritin than those with continuous fever. Patients with continuous fever had less increase in NLR than those with intermittent fever. Patients with intermittent fever had less increase in ESR than those with continuous fever.

Based on duration, fever is separated in three categories – acute (duration less than 7 days), sub-acute (duration 8 to 14 days), chronic (duration more than 14 days).

So, patients with sub-acute and chronic fever had more increase in CRP than those with acute fever. Patients with acute fever also had moderate increase in CRP. Patients with chronic fever had more increase in D-dimer than those with sub-acute and acute fever. But, patients with sub-acute and acute fever had significant rise of D-dimer. Patients with chronic fever had more increase in ferritin than those with sub-acute and acute fever. But, patients with sub-acute and acute fever had significant rise of ferritin. Patients with Sub-acute and chronic fever had more increase in NLR than those with acute fever. Patients with sub-acute and chronic fever had more increase in ESR than those with acute fever.

DISCUSSION

In this single-center and observational retrospective study, we have studied on the clinical and laboratory characteristics of 60 cases of SARS-CoV-2. Our main findings are as follows:

We found that patients with moderate and severe fever had higher CRP, ferritin and D-dimer than those with mild fever but again, NLR and ESR were more raised in patients with mild temperature. so, mild fever should not be neglected and full battery of inflammatory markers should be checked.

Also, high rise of CRP, ferritin and D-dimer is seen with intermittent fever but NLR and ESR were more increased in patients with continuous fever.

With longer duration of fever more severe response of CRP, ferritin, D-dimer, NLR and ESR is seen. So, early investigation and urgent intervention is required in a patient who presents with sub acute and chronic fever.

SARS-CoV-2 infection currently represents the worst global pandemic disease and efforts are being made worldwide to find a possible cure. Different research studies have focused on trying to identify the path physiology behind this disease¹⁴. It has been known that SARS-CoV-2 can initiate a strong harmful immune response in some patients¹⁵. However, its specific mechanism is not yet completely known.

Different studies have already shown that the SARSCoV-2 infection determines a higher production of inflammatory cytokines¹⁶. In particular, it has been seen that this immune response can either be helpful to fight the viruses¹⁷, or exacerbate the number of inflammatory chemokines leading to a process known as “cytokine storm,” that could worsen the patients’ already critical conditions.^{18, 19}

CONCLUSION

So, there are positive correlations between pattern of fever and biochemical inflammatory markers. Patients who present with mild or acute or continuous fever have different changes in biochemical markers than those with intermittent, sub acute, chronic or moderate-severe fever. Complete biochemical panel can show actual status of the patient. We should monitor all types of patients throughout the course of the disease.

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