Clinical manifestations, comorbidities and blood counts as markers of severity in COVID-19 patients in Babylon Province

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Abstract

Objective: With the pandemic of COVID-19 and increasing number of patients all over the world including our country (Iraq), there is a need to investigate the clinical features, comorbidities and hematological parameters for risk stratification.

Methods: A cross-sectional study involved 151 patients diagnosed as COVID-19 by Polymerase chain reaction. Data were studied regarding the effect of demographic features, comorbidities and blood indices including neutrophil, lymphocyte, monocyte, platelet, hemoglobin, neutrophil lymphocyte ratio, lymphocyte monocyte ratio and platelet lymphocyte ratio on disease severity.

Results: Mean age of patients was 37. 8 ± 18. 77, 4 patients were health workers, 79. 5% gave history of contact with infected patients. Most common symptoms were fever 90. 1%, cough 84. 8% and shortness of breath 31. 1%. 78. 8% had normal neutrophil count,71. 6% had normal lymphocyte count, 87. 5% had normal platelet count, 82. 1% had positive results for C-reactive protein. Disease was significantly more severe with increasing age, smoking, presence of shortness of breath, fatigue, loss of smell and more severe in the presence of comorbidities (hypertension, diabetes mellitus, respiratory disease, renal disease, heart disease and malignancy) and more severe with decrease platelet counts and increase neutrophil lymphocyte ratio.

Conclusion: Most patients give history of contact reflecting wide spread of disease. Neutrophil, lymphocyte and platelet counts are of little value for confirming the disease. More care needs to be taken when deal with patients whom they have increasing age, smoking, shortness of breath, presence of comorbidities and increase neutrophil lymphocyte ratio.

1. Introduction

The 2019 coronavirus disease (COVID-19) was the cause of unexplained viral pneumonia in Wuhan, China in December 2019, and was reported to spread throughout the Hubei Province and China in the following month and even to other countries [1], causing 34,662 confirmed cases of infection by 8 February 2020, so the World Health Organization considered coronavirus disease as a pandemic in March 11,2020 after a series of confirmed cases that exceeded 300,000 people worldwide and about 14,500 deaths.

Coronaviruses are large (28–32 kb) single-stranded positive-sense RNA viruses [2]. Coronavirus attaches to its receptor, dipeptidyl peptidase 4 to enter host cells. Then, protease cleavage of the S protein is required for virus–cell fusion and release of genomic RNA into the cytoplasm. Coronaviruses are characterized by high rates of mutation and recombination and a propensity to cross host species [2]. Dipeptidyl-peptidase 4 (DPP4, also known as CD26) was identified as the host-cell receptor for cell entry [3]. COVID-19 virus is transmitted through respiratory droplets and contact routes [4]. Airborne transmission was not reported in an analysis of 75,465 COVID-19 cases in China. Droplet transmission occurs when a person is in close contact (within 1 meter) with a person who has respiratory symptoms (e. g. , coughing or sneezing) and is therefore at risk of having his/her mucosa (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets [5].

Studies about COVID-19 epidemiological and clinical characteristics show that COVID-19 patients may develop either mild or severe symptoms of acute respiratory infection, the mild symptoms include fever, dry cough, fatigue abnormal chest CT findings but the prognosis is good [6, 7]. In contrast, patients with severe symptoms may develop severe pneumonia, acute respiratory distress syndrome (ARDS) or multiple organ failure. The death rates are ranging between 4. 3 % to 15 % according to different study reports [6, 8]. Inflammation resulted in infectious diseases, and growing evidence supports its significant role in the progression of various viral pneumonia [9]. Severe inflammatory responses lead to weak adaptive immune response, thereby resulting in immune response imbalance. So, circulating biomarkers that can represent inflammation and the immune status are prognostic potential predictors for COVID-19 patients [10].

There are many studies suggest that complete blood count is beneficial in diagnosis of COVID-19 or predicts it`s severity. There are many abnormal hematological parameters reported in patients with COVID-19, these parameters include changes in blood element count including lymphocyte count, neutrophil count, monocyte count, platelet count and the ratio between these parameters in addition to changes in D-dimer, lactic dehydrogenase, ferritin and fibrinogen, but the clinical use of these indices remain evasive [11, 12]. The neutrophil to lymphocyte ratio (NLR) is an accordant index that can be calculated from a complete blood count, and its prognostic value are showed in many studies in various conditions, including sepsis, cardiovascular diseases, and malignant tumors, and its role in COVID-19 needs to be more clarified [13, 14].

2. Aim of study

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To study the demographic and characteristic features of patients infected with COVID-19 and the effect of comorbidities on the disease severity and to study the value of complete blood count including neutrophil count, lymphocyte count, monocyte count, platelet count, hemoglobin, neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR) in assessing the severity of disease.

Patients and methods

Prospective observational study involved patients diagnosed to have COVID-19 who had been admitted to Merjan Teaching Hospital and Al-Hilla Teaching Hospital (infectious ward) from 1/6/2020 to 23/6/2020.

All patients had positive results for COVID-19 by real time PCR of nasal and pharyngeal specimen. Patients were randomly selected.

Careful history was taken including epidemiological history (history of travel, history of contact with infected patients), also history was taken regarding demographic characteristics including age, gender, residence and smoking habit. History of comorbidities was taken from the patients including history of diabetes mellitus, hypertension, heart disease and malignancies, and then symptoms of patients were reviewed including fever, cough, shortness of breath, fatigue, headache, loss of smell and gastrointestinal tract symptoms. Radiological imaging was taken for the patients including chest X-ray and chest CT scan. Asymptomatic patients were not usually sent for radiological imaging. Because of the load on CT scan, some of mild patients were also not sent for CT scan especially if they were improving. Some of the patients were sent for CT scan before getting the results of PCR and others after the appearance of the results of PCR to assess the severity of disease and plan for treatment. After that patients were classified into asymptomatic and symptomatic, symptomatic patients were classified as follows:

1. Mild: slight clinical symptoms, no pneumonia manifestation.
2. Moderate: with fever, respiratory tract symptoms and imaging showed lung involvement.
3. Severe: if the patients got:a. respiratory distress, respiratory rate ≥ 30 breath/minute, b. in the resting state mean O_2 saturation ≤ 93%.
4. Critical: if the patients got: a. respiratory failure occurred and required mechanical ventilation, b. shock occurred, c. intensive care unit (ICU) admission was required for combined organ failure [15].

The patients were sent for complete blood count including neutrophil, lymphocyte, monocyte, hemoglobin and platelet in automated machine which gives normal values as follows: neutrophil: 1. 63- 6. 96 (10^9/L), lymphocyte: 1. 09- 2. 99 (10^9/L), monocyte: 0. 240 -0. 790 (10^9/L), Hb: 12. 5 – 16. 0 g/dl, platelet: 150- 450 (10^9/L).

Requirement for oxygen was assessed, whether they did not require oxygen or required oxygen only or required mechanical ventilation. Patients were followed till recovery or death, criteria for recovery included 2 negative PCR 24 hours interval after 3days free from symptoms or the patients got no symptoms for more than 10 days without the need for PCR.

3. Data Analysis

Statistical analysis was carried out using SPSS version 23. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means ± SD). Student t-test was used to compare means between two groups. Chi-square test and Fisher-exact test were used to find the association between categorical variables. A *p*-value of ≤ 0. 05 was considered as significant.

Results

The study was conducted in Merjan Teaching Hospital and Al-Hilla Teaching Hospital (infectious ward) from 1/6/2020 to 23/6/2020 included 151 patients, mean age 37. 80 ±18. 77 ranged from 5 years to 85 years, 4 patients (2. 6%) of them were medical health workers (1 patient was a doctor and 3 patients were nurses). 120 patients (79. 5%) gave history of contact with positive patients, while 31 patients (20. 5%) did not give history of contact with positive patients, no patient gave history of travel outside the country.

Table 1: Distribution of patients according to demographic features and clinical characteristics (n=151)

	N	Percentage
Gender		
Female	65	43.0%
Male	86	57.0%
Total	151	100.0%
Residence		
Center	86	64.2%
Periphery	54	35.8%
Total	151	100.0%
Smoking habit	48	31. 8%
Comorbidities:		
Hypertension	56	37. 1%
Diabetes mellitus	39	25. 8%
Respiratory diseases	16	10. 6%
Renal diseases	19	12. 6%
Heart diseases	31	20. 5%
Malignancy	11	7. 3%
Symptoms:		
Fever	136	90. 1%
Cough	128	84. 8%
Shortness of breath	47	31. 1%
Fatigue	53	35. 1%
Headache	64	42. 4%
Loss of smell	6	4. 0%
Gastrointestinal tract manifestation	18	11. 9%
Respiratory support		
None	109	72. 2%
O2	37	24. 5%
Mechanical ventilation	5	3.3%

From 16 patients whom they had respiratory disease, 11 patients had chronic obstructive airway disease, 5 patients had asthma, out of 31 patients with cardiac disease there were 9 patients with heart failure and 22 patients with ischemic heart disease, there were 19 patients with chronic renal failure (9 patients of them on hemodialysis), from 11 patients with malignancy there were 3 patients with lung cancer, 4 patients had lymphoma, 2 patients had renal cell carcinoma and 2 patients had gastrointestinal malignancy.

Table 2: Distribution of patients according to blood counts (n=151):

Study variables	(Mean ± SD)	Range	Normal ranges

Neutrophil	(4. 49 ± 3. 16)	(1. 24-21. 0)	1. 63-6. 96(10^9/L)
Lymphocyte	(1. 78 ± 1. 08)	(0. 336-9. 8)	1. 09-2. 99(10^9/L)
Monocyte	(0. 37 ± 0. 16)	(0. 12-0. 954)	0. 240-0. 790(10^9/L)
Hb	(13. 65 ± 1. 81)	(8. 68-18. 9)	12. 5-16 g/dl
Platelet	(219. 56 ± 79. 60)	(15. 2-676. 0)	150-450(10^9/L)
NLR	(3. 52 ± 3. 89)	(0. 38-19. 79)	-
PLR	(148. 17 ± 80. 95)	(22. 62-464. 29)	-
LMR	(5. 35 ± 3. 23)	(0. 61-21. 05)	-

Out of 151 patients, 22 patients (14. 6%) had neutrophil count > 6. 96 and 11 patients (7. 3%) had neutrophil count < 1. 63. Out of 151 patients, 12 patients (7. 9%) had lymphocyte count > 2. 99 and 31 patients (20. 5%) had lymphocyte count < 1. 09. Out of 151 patients, 1 patient (0. 6%) had platelet count > 450 and 18 patients (11. 9%) had platelet count < 150. There were 124 patients (82. 1%) with positive results for CRP, while there were 27 patients (17. 9%) with negative results for CRP.

The number of patients that were classified as asymptomatic/mild was 109 patients (72. 2%), only 8 patients (5. 2%) of them were asymptomatic while 101 patients (66. 8%) were classified as having mild disease. The number of patients that were classified as moderate/severe was 42 patients (27. 8%) including critical patients with them,20 patients (13. 2%) were moderate, 16 patients (10. 6%) were severe and 6 patients (3. 9%) were critical.

There was significant association between severity of infection and age as shown in table 3.

Table 3: The association between severity of infection and age:

Study variables	Severity	N	Mean	SD	t-test	P-value
Age (years)	Mild /asymptomatic	109	34.23	17.21	-3.93	<0.001*
	Moderate / severe	42	47.04	19.70		

Table 4: shows the association between severity of infection including (mild/ asymptomatic and moderate/ severe) and study variables including (gender, residence, smoking habit, symptoms and comorbidities). There were significant association between severity of infection and smoking habit, shortness of breath, fatigue, loss of smell, hypertension, diabetes mellitus, respiratory disease, renal disease, heart disease and malignancy.

Table 4: The association between severity of infection and demographic features, symptoms and comorbidities:

Study variables	Severity of infection		Total	χ^2	P-value
	mild/ asymptomatic	moderate/ severe			
Gender					
Female	51 (46. 8%)	14 (33. 3%)	65 (43. 0%)	2. 239	0. 135
Male	58 (53. 2%)	28 (66. 7%)	86 (57. 0%)		
Total	109 (100. 0%)	42 (100. 0%)	151 (100. 0%)		
Residence					
Center of Hilla	67 (61. 5%)	30 (71. 4%)	97 (64. 2%)	1. 309	0. 253
Periphery of Babylon	42 (38. 5%)	12 (28. 6%)	54 (35. 8%)		
Total	109 (100. 0%)	42 (100. 0%)	151 (100. 0%		
Smoking habit	29 (26. 6%)	19 (45. 2%)	48 (31. 8%)	4. 854	0. 028*
Fever	97 (89. 0%)	39 (92. 9%)	136 (90. 1%)		0. 561 f
Cough	93 (85. 3%)	35 (83. 3%)	128 (84. 8%)	0. 093	0. 761
Shortness of breath	5 (4. 6%)	42 (100. 0%)	47 (31. 1%)	128. 74	<0. 001*
Fatigue	30 (27. 5%)	23 (54. 8%)	53 (35. 1%)	9. 875	0. 002*
Headache	47 (43. 1%)	17 (40. 5%)	64 (42. 4%)	0. 087	0. 768
Loss of smell	1 (0. 9%)	5 (11. 9%)	6 (4. 0%)		0. 007 * f
Gastrointestinal manifestation	11 (10. 1%)	7 (16. 7%)	18 (11. 9%)	1. 248	0. 264
Hypertension	33 (30. 3%)	23 (54. 8%)	56 (37. 1%)	7. 79	0. 005*
DM	18 (16. 5%)	21 (50. 0%)	39 (25. 8%)	17. 74	<0. 001*
Respiratory diseases	2 (1. 8)	14 (33. 3)	16 (10. 6)		<0. 001*f
Renal diseases	5 (4. 6)	14 (33. 3)	19 (12. 6)	22. 77	<0. 001*
Heart diseases	15 (13. 8%)	16 (38. 1%)	31 (20. 5%)	11. 00	0. 001*
Malignancy	2 (1. 8%)	9 (21. 4%)	11 (7. 3%)		<0. 001*
Outcome of the patients					
Recover	108 (99. 1%)	37 (88. 1%)	145 (96. 0%)		
Dead	1 (0. 9%)	5 (11. 9%)	6 (4. 0%)		0. 007* f
Total	109 (100. 0%)	42 (100. 0%)	151 (100. 0%)		
Need for respiratory support					
O^2	1 (0. 9%)	36 (85. 7%)	37 (24. 5%)		<0. 001* f
Mechanical ventilation	0 (0. 0%)	5 (11. 9%)	5 (3. 3%)		
*p value ≤ 0. 05 was significant.					

Table 5 shows the mean differences of study variables including (neutrophil, lymphocyte, monocyte, Hb, Platelet count, NLR, PLR and LMR) according to severity of infection including (mild/ asymptomatic and moderate/ severe). There were significant differences between means of platelet count and NLR to severity of infection.

Table 5: The mean differences of blood counts according to severity of infection:

Study variables	Severity	N	Mean	SD	t-test	P-value

Neutrophil	Mild /asymptomatic	109	4. 24	2. 74	-1. 323	0. 191
	Moderate / severe	42	5. 14	4. 03		
Lymphocyte	Mild /asymptomatic	109	1. 87	1. 17	1. 591	0. 114
	Moderate / severe	42	1. 56	0. 79		
Monocyte	Mild /asymptomatic	109	0. 36	0. 15	-0. 855	0. 394
	Moderate / severe	42	0. 39	0. 17		
Hb (g/l)	Mild /asymptomatic	109	13. 61	1. 73	-0. 415	0. 679
	Moderate / severe	42	13. 75	2. 02		
Platelet	Mild /asymptomatic	109	227. 73	80. 60	**2. 053**	**0. 042***
	Moderate / severe	42	198. 36	73. 69		
NLR	Mild /asymptomatic	109	3. 02	3. 10	**-2. 06**	**0. 044***
	Moderate / severe	42	4. 81	5. 26		
PLR	Mild /asymptomatic	109	149. 31	86. 00	0. 278	0. 782
	Moderate / severe	42	145. 21	66. 94		
LMR	Mild /asymptomatic	109	5. 59	3. 30	1. 445	0. 15
	Moderate / severe	42	4. 74	2. 99		
*P value ≤ 0. 05 was considered as significant.						

Table 6 shows the mean difference of CRP according to severity of infection including (mild/ asymptomatic and moderate/ severe) which shows no significant difference.

Table 6: The mean difference of CRP to severity of infection:					
Study variables	**Severity of infection**		**Total**	**χ2**	**P-value**
	mild/ asymptomatic	**moderate/ severe**			
CRP results					
Positive	87 (79. 8)	37 (88. 1)	124 (82. 1)	1. 415	0.234
Negative	22 (20. 2)	5 (11. 9)	27 (17. 9)		
Total	109 (100. 0)	42 (100. 0)	151 (100. 0)		

145 patients (96%) recovered and unfortunately 6 patients (4%) died (2females and 4males),the mean age of dead patients was 45. 83 ±SD 18. 62 (youngest patient was 22 years old and oldest patient was 70 years old).

Table 7: distribution of dead patients according to smoking and comorbidities:		
Study variables	**Number**	**Percentage**
Smoking habit	2	(33. 3%)
Fever	5	(83. 3%)
Cough	5	(83. 3%)
Shortness of breath	6	(100. 0%)
Fatigue	3	(50. 0%)
Headache	2	(33. 3%)
Loss of smell	1	(16. 7%)
Gastrointestinal tract manifestation	0	(0. 0%)
Hypertension	3	(50. 0%)
Diabetes mellitus	5	(83. 3%)
Respiratory diseases	3	(50. 0%)
Renal diseases	1	(16. 7%)
Heart diseases	3	(50. 0%)
Malignancy	3	(50. 0%)
Need for respiratory support		
O^2	1	(16. 7%)
Invasive ventilation	5	(83. 3%)

All the dead patients had comorbidities, 2 patients had one comorbidity while the other 4 patients had more than one comorbidity.

Table 8: distribution of dead patients according to blood count elements:		
Study variables	**Mean**	**SD**
Neutrophil	11. 21	7. 09
Lymphocyte	1. 02	0. 41
Monocyte	0. 61	0. 19
Hb (g/l)	13. 43	2. 99
Platelet	186. 15	114. 49
NLR	10. 65	8. 00
PLR	184. 43	126. 07
LMR	1. 81	0. 81
Hb (g/l)	13. 43	2. 99

4. Discussion

Since the discovery of the first case of COVID-19 in Babylon province at the end of February 2020, there is increasing number of detected cases of COVID-19, and this number is increasing rapidly by the end of May and the beginning of June 2020 and associated with increasing mortality. There is a difficulty facing the medical staff and that is the shortage of medical resources, especially critical case resource, and for this reason identification of critical illness and risk stratification can help in detecting serious patients and might reduce mortality. So it seems very important to detect markers of severity of the illness in order to detect early patients whom are suspected to get their illness to be severe and to take more care with them.

This study showed that the mean age of patients was 37. 80 ± 18. 77 ranged from 5 years to 85 years, while other studies showed that the mean age was 63 years [16] and another study showed that the(mean [SD] age, 57. 5± 16. 8 years) [17] (these studies were done in USA), another studies in China showed that mean ages were 40 years, 47 years and 50 years [11, 15, 18], the mean age in this study was less in comparison with other studies probably because the life span of the Iraqi people is less than these societies and more younger people are present in our society.

There were 4 (2. 6%) medical healthcare workers (1 patient was a doctor and 3 patients were nurses). Medical health workers are more liable to get the disease due to their close contact with patients, so all the measures need to be taken to protect themselves from getting the disease.

This study showed that most patients (79. 5%) gave history of contact with positive patients and this reflect the spread of disease in our society and no patient gave history of travel outside the country because the boundaries were closed at that time and there was restriction of travelling outside the country.

In this study there were 86 (57%) males while there were 65 (43%) females, in comparison with other studies, a total of five studies were included [6, 8, 19-21], the results of the randomized effects model meta-analysis showed that regarding gender distribution male accounted 60% of COVID-19 patients, which was higher than women. There are some studies that showed MERS-COV and SARS-COV have also been found to infect males more than females [22, 23]. The reduced susceptibility of females to viral infections could be attributed to the protection from X chromosome and sex hormones, which play an essential role in innate and adaptive immunity [24], or because of the life style in our society that makes male do their work outside their houses so that they are more liable to get contact with the society.

Most of patients came from center of Babylon province from Al Hilla city being it is the largest city in Babylon province and most crowded.

This study showed that the percentage of comorbidities were: hypertension (37. 1%), diabetes mellitus (25. 8%), respiratory disease (10. 6%), renal disease (12. 6%), heart disease (20. 5%) and malignancy (7. 3%).

In comparison with other studies the percentage given were: hypertension was found in 15. 8%, 15%, 15. 2% and 24. 41%, diabetes mellitus was found in 9. 4%, 20%, 7. 4% and 7. 87 %, respiratory diseases was found in 1. 4%, 2%, 1. 1% and 4. 72%, heart disease was found in 11. 7%, 15%, 2. 5% and 4. 72 %, malignancy was found in 1. 5%, 2%, 0. 9% and 3. 94 % [6, 11, 18, 25]. This difference in the percentage of comorbidities seems to be due to difference in the prevalence of comorbidities in different societies.

In this study the most common symptom was fever (90. 1%) followed by cough (84. 8%), headache (42. 4%), fatigue (35. 1%), shortness of breath (31. 1%), gastrointestinal symptoms (11. 9%) and loss of smell (4. 0%).

In comparison with other studies: fever was found in 70%, 98%, 82. 7%, 85% and 88. 7% [11, 18, 26-28], while cough was found in 48%, 83%, 72%, 82. 6% and 67. 8% [11, 18, 26-28] and shortness of breath was found in 32%,72%,5. 3%,7. 8% and 18. 7% [11, 18, 26-28].

In this study the percentage of fever and cough were high because most patients that had been included in this study had been already admitted and little asymptomatic patients were included in this study.

In spite that fever and cough were the most common manifestations of the disease but their absence don't exclude the diagnosis since there were 9. 9% of the patients with no fever and 15. 2% of the patients with no cough and so, high degree of suspicion is needed when deal with patients because the disease becomes common in our society.

Loss of smell was uncommon symptom in this study [6 patients (4. 0%)] probably because these patients were not aware of this complaint and they had other symptoms that dominate on it.

In this study 22 patients (14. 6%) had neutrophil count > 6. 96(10^9/L) and 11 patients (7. 3%) had neutrophil count < 1. 63(10^9/L), and 118 patients (78. 1%) with normal neutrophil count, 12 patients (7. 9%) had lymphocyte count > 2. 99(10^9/L) and 31 patients (20. 5%) had lymphocyte count < 1. 09(10^9/L) and 108 patients (71. 5%) had normal lymphocyte count, 1 patient (0. 6%) had platelet count > 450(10^9/L) and 18 patients (11. 9%) had platelet count < 150(10^9/L) and 132 patients (87. 5%) had normal platelet count, so neutrophil, lymphocyte and platelet counts seems to be invalid in confirming or excluding the diagnosis of the disease being that there were 78. 1% of patients with normal neutrophil count, 71. 5% of patients with normal lymphocyte count and 87. 5% of patients with normal platelet count, and also the finding of high or low counts of neutrophil, lymphocyte and platelet dose not confirm or exclude the diagnosis.

In this study the means of neutrophil, lymphocyte, monocyte and platelet were 4. 49(10^9/L), 1. 78(10^9/L), 0. 37(10^9/L) and 219. 56(10^9/L) respectively, in comparison with other studies the means of neutrophil, lymphocyte, monocyte and platelet were 2. 8(10^9/L), 0. 9(10^9/L), 0. 3(10^9/L) and 183. 1(10^9/L) respectively [29], and another study which showed that the means of neutrophil, lymphocyte and platelet were 3. 37(10^9/L), 1. 21(10^9/L) and 198(10^9/L) respectively [18].

There were 124 patients (82. 1%) with positive results for CRP, while there were 27 patients (17. 9%) with negative results for CRP, compared with other studies that were done in China reported that 58. 7% and 60. 7% of patients with COVID-19 had positive CRP levels [11, 28], the large percentage of positive CRP in this study seems to be due to that the patients included in the study were admitted patients whom they had more severe illness and CRP increases with increased severity of inflammation. In spite that most of the patients (82. 1% of them) had positive CRP still negative CRP results dose not exclude the diagnosis.

In this study there was significant association between severity of infection and age, and the age is an important prognostic factor. This is consistent with other studies [11, 29].

In this study there was significant association between severity of infection and smoking habit.

A study in China showed that the proportion of smokers was less than expected based on the estimated prevalence of smoking in the country [30]. Another study in New York for hospitalized patients with COVID-19 showed that the prevalence of smokers was 5. 1% which is less than half of the most recent estimate of the overall US smoking prevalence of 13. 7% [31]. A retrospective study done in Italy (similar to the study that done in New York) for 441 patients admitted to a hospital in northern

Italy, found that less than 5% of patients were smokers, compared to an estimated age-adjusted prevalence of 14. 9% [32]. In contrast, the most recent meta-analysis of 19 peer-reviewed papers that included 11,590 patients concluded that smoking is a risk factor for the progression of COVID-19, with smokers having higher odds of COVID-19 progression [33], and this is consistent with this study that found that smoking was a marker of severity.

In this study there was significant association between the severity of the disease and comorbidities (hypertension, diabetes mellitus, renal diseases, respiratory diseases, heart disease and malignancies) and this is consistent with other studies [11, 29, 34].

The study showed significant association between the severity of infection and symptoms (shortness of breath, fatigue and loss of smell).

In spite that 72. 2% of patients improved spontaneously and didn't require oxygen therapy, but oxygen therapy was important and required in 24. 5% of patients, mechanical ventilation was required in 3. 3% of patients making it vital to supply the hospitals with more of these machines.

In this study the mean lymphocyte count in moderate and severe cases was lower than that of mild and asymptomatic cases but it was statistically not significant and the mean level of neutrophil count was higher in moderate and severe cases than that of mild and asymptomatic cases but it was also statistically not significant but when the neutrophil to lymphocyte ratio was taken it was statistically significant more in moderate and severe cases than that of mild and asymptomatic cases.

Neutrophil is a major component of leukocyte population that migrates from the venous system to the affected organ. Neutrophil releases large amounts of reactive oxygen species that can damage the cell and free the virus from the cell and may kill the virus directly and stimulate cell specific antihumeral immunities [35].

Lymphocyte and endothelial cells produce virus-related inflammatory factors, such as interleukin-6 and interleukin-8, tumor necrosis factor-alpha and granulocyte colony stimulating factor, and interferon-gamma factors, which can trigger neutrophil [36-39]. All of the above factors results in increase neutrophil count.

It is not known why lymphopenia is associated with severe illness. It has been thought that COVID-19 act on T-lymphocyte, and T-lymphocyte damage is an important factor in the illness or in the deterioration of the patient's illness [40] The neutrophil to lymphocyte ratio (NLR) was used widely to assess the prognosis of patients with pneumonia and tumors and to assess the severity of bacterial infection [40-42]. So the neutrophil to lymphocyte ratio seems to be an important predictor of poor prognosis in patients with COVID-19 and this is consistent with other studies that put the cut of value of neutrophil to lymphocyte ratio in different figures. In one study the incidence of critically ill patients with neutrophil to lymphocyte ratio (NLR) more than 3. 13 and aged 50 years or more was 50% and it was 9. 1% in aged less than 50 years and neutrophil to lymphocyte ratio (NLR) less than 3. 13 [43], in another study the optimal threshold given for neutrophil to lymphocyte ratio was 3. 3 and this showed a superior prognostic possibility of clinical symptoms to change from mild to severe, when age ≥49. 5 years old and NLR≥3. 3, 46. 1% of the COVID-19 patients with mild disease will become severe. So, these patients must be closely attended by clinicians. By contrast, when age<49. 5 years old and NLR<3. 3, COVID-19 patients with mild disease can be cured and discharged at approximately 13. 5 days [44]. There are morphological and inflammation-related phenotypic changes in peripheral blood monocytes that correlates with the outcome of the patients, in which excessive monocyte-macrophage activation that occurs in severe illness lead to respiratory failure [45], but this study did not found significant association regarding the level of monocyte and severity of infection.

In this study CRP (which is an acute phase reactive protein and it reflects the severity of inflammation) showed no significant difference according to severity of infection and this is consistent with some studies [43]. While other studies showed that there was significant association between CRP and severity of infection [11, 29].

Six patients died, each one of them had one or multiple comorbidities. So the comorbidities were important as a marker for the severity of the illness especially if the patient had more than one comorbidity.

The mean neutrophil count of dead patients was high (11. 21×10^9/L), while the mean lymphocyte count was low (1. 02×10^9/L), and the neutrophil lymphocyte ratio for dead patients was high (10. 65) reflecting the importance of these parameters as a markers of severity of illness.

It is important to assess the patients initially to look for patients whom their disease may progress to severe illness and this criterion needs to include age, smoking, shortness of breath, fatigue, loss of smell, presence of comorbidities especially if more than one comorbidity, low lymphocyte count, high neutrophil count and high neutrophil to lymphocyte ratio and to put a point to each one of them to determine whom patient needs to get admission.

5. Conclusion

1. Most patients give history of contact reflecting the wide spread of the disease.
2. High degree of suspicion about the disease needs to be taken with patients even if they have no fever and cough.
3. Negative CRP dose not exclude the diagnosis.
4. Neutrophil, lymphocyte and platelet counts are of little value in confirming or excluding the diagnosis.
5. Increasing age and smoking are associated with more severe illness.
6. Comorbidities including diabetes mellitus, hypertension, renal diseases, heart disease, respiratory disease and malignancy are associated with more severe illness.
7. Shortness of breath, fatigue and loss of smell are associated with more severe illness.
8. Neutrophil to lymphocyte ratio is an important predictor of the severity of the illness.

6. Recommendation

1. Criterion needs to be put to evaluate the patients whom they are expected that their illness may progress to severe form.
2. More markers for severity needs to be studied and evaluated including serum troponin, serum ferritin, lactic dehydrogenase, D-dimer, chest CT findings and others.

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