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Research Paper

Evaluation of Haematological Parameters in Patients with Covid 19 Infection in Nineveh Province

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ABSTRACT:

BACKGROUND:

In December 2019, a novel virus later named severe acute respiratory syndrome coronavirus-2 was isolated from the broncho-alveolar fluid of a patient in Wuhan, suffering from what became known as coronavirus disease 2019 (COVID-19). The first case was registered in Nineveh Province on March 22, 2020. Diagnosis was made by molecular identification of severe acute respiratory syndrome coronavirus-2 by polymerase chain reaction. So, clinical, haematological, and haemoststic parameters should take in account as they are important in determining the severity of the illness and outcome. This study focus on haematological and some haemostatic parameters in 100 cases with positive polymerase chain reaction.

OBJECTIVE:

To evaluate the haematological parameters "CBC" in patients with COVID 19 infection and to study some of the changes in first line of coagulation parameters.

PATIENTS AND METHODS:

The current study is a case series study involving 100 patients admitted to Al-Shifaa hospital in Mousl city in the period between February 2021 and August 2021 involved collection of data, blood samples and laboratory investigations. The investigations include: complete blood count and coagulation parameters "prothrombin time (PT)" , "activated partial thromboplastin time (APTT)" , and "D.dimer".

RESULTS:

Out of 100 patients encompasses, 51 were males, 49 were females with the age range between 10-87 years. The patients presented with a wide range of symptoms, fever and cough were the most common complains. "Lymphopenia" was the most common haematological abnormality (74%). "D.dimer" was the most common coagulation abnormality (31%). Smokers run mild to moderate course of illness.

CONCLUSION:

Monitoring haematological and haemostatic parameters in patients with severe acute respiratory syndrome coronavirus-2 infection can predict the severity of the course of the disease and outcome of the patients.

KEY WORDS: CBC "complete blood count" , PT "prothrombin time" , APTT "activated partial thromboplastin time".

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INTRODUCTION:

Corona virus "SARS-COV-2" is a newly emerging, highly transmissible virus in humans. Until now, millions of infections and millions of deaths have been reported worldwide. In most cases, the disease is asymptomatic and self limited. A subset of infected subjects has severe symptoms and prolonged courses [(1)]. Around 10% of infected subjects need hospitalization and one third of them treated in intensive care units [(2)]. Coronaviruses are large enveloped, spherical, positive stranded RNA viruses associated with a nucleoprotein inside a capsid composed of matrix protein [(3)]. The envelope contains club shaped spike projections of glycoproteins which appear like a crown. The genome encodes four main proteins & accessory proteins. The spike protein composed of two subunits which cover the surface of the virus & attach to the host cells that display angiotensin converting enzyme 2(ACE2) receptors [4] [(5)] . Viral entry also depend on TMPRSS2 furin protease [(6)].

ACE2 & TMPRSS2 have been shown in nasal & bronchial epithelium by using immunohistochemistry so these cells implicate as loci of original infection & reservoir for dissemination [6]. Also, gene expression of ACE2 & TMPRSS2 has been detected in alveolar epithelial type 2 cells [7] [8]. The alveolar epithelial type 2 cells play a vital role in process of pathogenesis [9]. The virus transmitted by respiratory secretions & aerosols from infected person to healthy one. Once enter the body, the virus bind to host cells via receptors & then enter to cells by endocytosis[9]. Haematological changes are of important indices in COVID19 disease, and may be related to disease severity [2]. The patients classified according to American Thoracic Society and Infectious Diseases Society of America. Severe cases include either one major criterion or three or more minor criteria. Minor criteria are a respiratory rate > 30breaths/min, PaO2/FIO2 ratio < 250, multilobar infiltrates, confusion /disorientation, uremia, leucopenia, low platelet count, hypothermia, hypotension requiring aggressive fluid resuscitation. Major criteria comprise septic shock with need for vasopressors or respiratory failure requiring mechanical ventilation [2].

PATIENTS AND METHODS:

The current study is a case series study involving 100 patients admitted to Al Shifaa hospital in Mousl city in the period between February 2021 and August 2021 involved collection of data, blood samples and doing the laboratory investigations. A questionnaire was used for each individual and each person's name, age, sex were recorded, also the patient's symptoms including: fever, headache, muscle ache, cough, dyspnea, chest pain, anosmia, ageusia, gastrointestinal symptoms, and skin rash were recorded, also, we ask the patients about any history of contact, and smoking. The patients underwent haematological and coagulation investigations including "complete blood count" using Mythic Coulter (Orphee Medical), "d.dimer" using D.dimer(CLIA) kit from Clia Maglumi 800 (Snibe) , "prothrombin time" using BIO-TP kit from BIOLABO, and "activated partial thromboplastin time" using BIO-CK kit from BIOLABO. All statistical analyses were performed using SPSS software.

Chi-square was used to compare categorical variables. T test was used to compare continuous variables. P values < 0.05 were taken as statistical significant.

RESULTS:

Out of 100 patients, 51 (51%) were males & 49 (49%) were females, with the age range between 10-87 years. The cases were classified according to American Thoracic Society and Infectious Diseases Society of America. Fever and cough were the main clinical finding , table (1). Comparison between three groups of cases according to severity in relation to clinical parameters, table (2). Fever, cough, chest pain, and dyspnea were significantly seen in moderate and severe cases with P value 0.00, 0.00, 0.00, and 0.00, 0.00 respectively. Skin rash was significantly seen in severe cases with P value 0.00.

Concerning haematological finding, anemia was observed in 23/100 (23%) of patients ranging between mild & moderate anemia. Ten cases have hypochromic microcytic anemia, and the remaining presented with normochromic normocytic anemia. White blood cell count decreased in 3/100 (3%) of patients, also "lymphopenia", "relative neutrophilia", "thrombocytopenia" were observed, table (3). "Neutrophils count" was significantly higher in severe cases in comparison to mild and moderate with P value <0.00, while there was no significant finding regarding other parameters. "Platelets count" was significantly low in patients with low WBC, with P value 0.005, while there was no significant finding regarding other parameters. Comparison between three groups of cases according to severity in relation to haematological parameters, table (4).

"D.dimer" was elevated in 31/100 (31%) of patients. "Prothrombin time" (PT) was prolonged in 1/100 (1%) of patients. "Activated partial thromboplastin time" (APTT) was prolonged in 3/100 (3%) of patients seen in table (5). There was no significant difference between three groups regarding "D.Dimer", "prothrombin time (PT)", "activated partial thromboplastin time (APTT)" table[6]. "D.dimer" was significantly high in patients with low Hb with P value 0.02, while there was no significant finding regarding other parameters. Cases with history of smoking had significantly mild course of the disease with P value 0.00.

Table 1: Descriptive table of clinical parameters in all patients with SARS-COV-2 infection.

Clinical parameter	Male(%) n=51	Female(%) n=49	Total (%) n=100
Fever	41%	34%	75%
Cough	38%	32%	70%
Anosmia	31%	31%	62%
Ageusia	31%	31%	62%
Chest pain	31%	25%	56%
Dyspnea	26%	19%	45%
Headache	15%	15%	30%
Muscle ache	12%	12%	24%
GIT	12%	7%	19%
Skin rash	7%	1%	8%

Table 2: Comparison between three groups of cases according to severity in relation to clinical parameters according to American Thoracic Society and infectious Diseases Society of America

Clinical parameters		Mild n=57		Moderate n=28		Severe n=15		P value
		No.	%	No.	%	No.	%	
Fever	-ve	23	23%	1	1%	1	1%	0.00
	+ve	34	34%	27	27%	14	14%	
Headache	-ve	37	37%	23	23%	10	10%	0.235
	+ve	20	20%	5	5%	5	5%	
Muscle ache	-ve	43	43%	18	18%	15	15%	0.033
	+ve	14	14%	10	10%	0	0%	
Cough	-ve	28	28%	1	1%	1	1%	0.00
	+ve	29	29%	27	27%	14	14%	
Dyspnea	-ve	55	55%	0	0%	0	0%	0.00
	+ve	2	2%	28	28%	15	15%	
Chest pain	-ve	42	42%	2	2%	0	0%	0.00
	+ve	15	15%	26	26%	15	15%	
Anosmia	-ve	17	17%	14	14%	7	7%	0.116
	+ve	40	40%	14	14%	8	8%	
Ageusia	-ve	17	17%	14	14%	7	7%	0.116
	+ve	40	40%	14	14%	8	8%	
GIT	-ve	48	48%	25	25%	8	8%	0.011
	+ve	9	9%	3	3%	7	7%	
Skin rash	-ve	57	57%	27	27%	8	8%	0.00
	+ve	0	0%	1	1%	7	7%	

Table 3: Descriptive table of haematological parameters in all patients with SARS-COV-2 infection.

Haematological parameters	Minimum	Maximum	Median	Mean ± SD
Hb (g/dl)	8.0	16.6	12.5	12.6 ± 1.61
HCT (%)	24	56	37	38.28 ± 5.04
WBC (x10^9/L)	3.0	10	6.5	7.11 ± 2.17
Neutrophils %	46	94	78	76.2 ± 9.61
Lymphocytes %	4	47	15	18.2 ± 9.25
Platelets (x10^9/L)	87	415	184.00	188.4 ± 69.64

Table 4: Comparison between three groups of cases according to severity in relation to haematological parameters.

Haematological parameters		Mild n=57		Moderate n= 28		Severe n=15		P value
		No.	%	No.	%	No.	%	
Hb (g/dl)	Low <11.5	11	11%	5	5%	7	7%	0.096
	Normal	44	44%	20	20%	8	8%	
	High >16	2	2%	3	3%	0	0%	
HCT (%)	Low <37	31	31%	16	16%	8	8%	0.933
	Normal	25	25%	12	12%	7	7%	
	High >50	1	1%	0	0%	0	0%	
WBC (x10^9/L)	Low <4	2	2%	2	2%	1	1%	0.743
	Normal (4-10)	55	55%	26	26%	14	14 %	
Neutrophils (40-80%)	Normal	48	48%	18	18%	5	5%	0.000
	High	9	9%	10	10%	10	10 %	
Lymphocytes (20-40%)	Low	41	41%	20	20%	13	13 %	0.622
	Normal	14	15%	7	7%	1	1%	
	High	2	2%	1	1%	1	1%	
Platelets (x10^9/L)	Low <150	11	11%	14	14%	4	4%	0.096
	Normal (150-400)	45	45%	14	14%	11	11 %	
	High >400	1	1%	0	0%	0	0%	

Table 5: Descriptive table of coagulation parameters in all patients with SARS-COV-2 infection.

Coagulation parameters	Minimum	Maximum	Median	Mean ± SD
D.dimer (ng/ml)	51	7066	327	879.2 ± 1537.2
PT (second)	12.5	25	13	13.45 ± 1.32
APTT (second)	21	45	29	30.18 ± 4.82

Table 6: Comparison between three groups of cases according to severity in relation to coagulation parameters.

Coagulation parameters		Mild n=57		Moderate n=28		Severe n=15		P value
		No.	%	No.	%	No.	%	
D.dimer (ng/ml)	Normal	40	40%	21	21%	8	8%	0.340
	High >500	17	17%	7	7%	7	7%	
PT (second)	Normal (11-15)	56	56%	28	28%	15	15%	0.679
	High >15	1	1%	0	0%	0	0%	
APTT (second)	Normal (26-40)	55	55%	27	27%	15	15%	0.508
	High >40	2	2%	1	1%	0	0%	

DISCUSSION:

The age of majority of the patients in this study was above 40 years, and ranged between 10-87 years, with male predominance (51%). Two studies from USA, Arentz M et al and Bhatarju P et al including 21, 24 cases. The median of age was 58 and 51.9 years respectively. The age ranged from 22-95 years and 23-97 years respectively. Both studies showed a male predominance (82.1%) and (70%) [14,15]. Two studies from India, Anurag A et al [16] , and Patel K et al [17] , the median ages of these studies were 42.6, and 49 respectively. All these studies showed a male predominance (58.8% , 70%) respectively. Another indian study by Agrawal A et al [18] shows lower median age 32.5.

Patients infected with "COVID 19" present a wide range of symptoms. In this study fever was the most common symptom. Many studies showed compatible results like Kantri A et al [19], Rosa et al [20], Shi et al [21] , and Guan W et al [10] :Kantri A et al found that fever (45.5%) was the most frequently observed symptom, followed by dry cough (44%) and dyspnea (29%). Rosa R et al found that fever was seen in 58.6%, malaise 29.7%, dry cough 58.52%, dyspnea 30.82%, chest pain 11.49%, gastrointestinal symptoms like nausea and /or vomiting 7.33%, diarrhea 9.59%, abdominal pain 5.07%. Shi S et al found that fever was seen in 80.3%, cough 34.6%, dyspnea 28.1%. Guan W et al found that fever was seen in 43.8% of patients at admission and 88.7% during hospitalization, cough 67.8%, and diarrhea 3.8%. Neurological manifestation including dizziness 11.3%, confusion 5.75%, headache 12.17%, ageusia 19.6%, anosmia 15.4%, stroke 13%, and ataxia 2.1% were seen by Yassin A et al [22].

In this study, the mean "haemoglobin concentration" is 12.6 gm/dl. Mild and moderate anemia was reported in 23% of patients. No significant change in "haemoglobin concentration" in relation to severity. In studies done by Guan W et al [10], Huang C et al [23], Young B et al [24], Fan B et al [25], Zhou F et al [26], Liu Y et al [27], and Chen N et al [28], "haemoglobin concentration" were 13.4, 12.6, 13.5, 14.2, 12.8, 12.8, 14.8 gm/dl respectively. Agrawal A et al [18] demonstrated that "haemoglobin concentration" was 13.85 gm/dl in symptomatic patients. Lower result seen by Patel K et al [17] showed that "haemoglobin concentration" was 11.85 gm/dl.

The median "WBC count" was $6.5x10^9$/L. "Leucopenia" was observed in 5 cases (5%). No significant change in "WBC count" in relation to severity. The same result seen in Huang C et al [23], the median of total "WBC count" was $6.2x10^9$/L and In Zhou F et al [26] $6.2x10^9$/L. Lower count seen by Wang D et al [29] $4.5x10^9$/L, Wu C et al [30] $5.94x10^9$/L, Young B et al [24] $4.6x10^9$/L, and Fan B et al [25] $4.7x10^9$/L, higher count seen in Bhatarju P et al [15] was $8.4x10^9$/L. In Anurag A et al [16] and Agrawal A et al [18] from India the mean total "WBC count" $8.6x10^9$/L and $7.1x10^9$/L respectively. Patel K et al [17] found that the median "WBC count" $7.3x10^9$/L. Chen N et al [28] found that 9 cases (9%) with leucopenia.

Twenty nine of cases (29%) had "neutrophilia". "Neutrophils count" was significantly higher in severe cases than in mild and moderate cases with P value <0.00. Huang C et al [23] study from China found that the median of "absolute neutrophil

count" was $5x10^9$/L. The same result found by Wang D et al [29] . In Wu C et al [30] was $4.47x10^9$/L, in Young B et al [24] was $2.7x10^9$/L, and In Fan B et al [25] was $2.6x10^9$/L. Chen N et al [28] reported that the median "absolute neutrophil count" was $5x10^9$/L, and 38 cases (38%) had "neutrophilia". In Patel K et al [17] the median "absolute neutrophil count" was $6.8x10^9$/L.

"Lymphopenia" was seen in 74% of cases. No significant change in "lymphocyte count" in relation to severity. Similar results seen in Guan W et al [10] which found that "lymphopenia" present in 83.2% of the patients at admission, in Huang C et al [23] "lymphopenia" was seen in 63% of patients with "absolute lymphocyte count" $<1.0x10^9$/L , in Yang X et al [31] study from China "lymphopenia" was seen in 85% of patients. "Lymphopenia" also observed in Wang D et al [29] in 70.3%. Wu C et al [30] reported "lymphopenia" in 64% of patients. Arentz M et al [14] and Bhatraju P et al [15] showed "lymphopenia" in 67% and 75% of cases respectively. While other studies showed that appearance of "lymphopenia" at a lower rate like in Young B et al [24] "lymphopenia" was seen in 40% of patients, in Fan B et al [25] "lymphopenia" was seen in 36.9% of patients, in Zhou F et al [26] showed "lymphopenia" in 40% of cases, in Chen N et al [28] found that the median of "absolute lymphocyte count" was $0.9x10^9$/L with 35% having "lymphopenia", and In Patel K et al [17] found that "lymphopenia" was reported in 36% of patients.

The median "platelets count" was $184x10^9$/L, with 27% of cases had "thrombocytopenia". No significant change in "platelets count" in relation to severity. "Platelets count" was significantly low in patients with low "WBC count" with P value 0.005. The same result seen by Guan W et al [10] which found that the median "platelets count" was $168x10^9$/L with 36.2% of cases had "thrombocytopenia", In Liu Y et al [27]was $160.3x10^9$/L, with 8.3% had "thrombocytopenia", in Huang C et al [23] was $164.5x10^9$/L, with 4.9% of cases had "thrombocytopenia", In Wang D et al [29] was $163x10^9$/L, and in Young B et al [24] was $159x10^9$/L. Agrawal A et al [18] found that the mean "platelets count" was $183x10^9$/L in symptomatic patients. In Patel K et al [17] the "platelets count" ranged between $90\text{-}149x10^9$/L, with 32% had "thrombocytopenia". Other studies showed higher results, Fan B et al [25] was $201x10^9$/L, with 20% had "thrombocytopenia", In Zhou F et al [26] was $206x10^9$/L, with 7% had "thrombocytopenia", and in Chen N et al [28] $213x10^9$/L, with 12% had "thrombocytopenia".

The mean "PT" in this study was near to the finding by Wang D et al [29] 13.2s, Peng YD et al [32] 13.9s, and Huang C et al [23]12.2s. Different results seen by Wan S et al [33] when "PT" was 11.3s , and in Wu C et al [30] was 11.7s.

The mean "APTT" was similar to Wang D et al [29] 30.4s and Wan S et al [33] 29.7s. More prolongation seen by Peng YD et al [31] 36.5s, while Huang C et al [23] and Wu C et al [30] showed lower results "APTT" 26.2s, 26s respectively.

"D.dimer" was elevated in 31% of cases with mean 879.2 ng/ml. This is compatible with Wan S et al [33], Mao L et al [34], Wu C et al [30], and Liu Y et al [27] with mean "d.dimer" 600 , 900, 1200, 1500 respectively. Higher levels seen by Huang C et al [23], while, Wang D et al [29] found that the mean "d.dimer" was 400ng/ml. similar result seen by Zhang J et al [35] . "D.dimer" was significantly increased in patients with low haemoglobin compared with those with normal haemoglobin with P value 0.02. this is may be due to strong inflammatory response that affects, erythropoiesis leading to anaemia and abnormal coagulation process leading to elevated "D.dimer" [36] .

Mohsin F et al [37] found that smoking fuels the progression of COVID 19 severity, analysis found that severe smokers are at 2.45 times higher risk of having critical illness. Zhao Q et al [38], and Cen Y et al [39]also found that smokers with a longer active smoking are more prone to severe infection with "SARS-COV-2". Meta-analysis by Lippi G et al [40] was performed including 5 studies, in only one study active smoking was found to be significant predictor of severity, while, in the remaining four studies the association was not statistically significant (P value 0.254). No significant association was found by large study by Guan W et al [10] (P value 0.24). In this study, smoker COVID 19 patients had a mild course of illness with P value 0.00. This is due to decreased levels of angiotensin converting enzyme 2 (ACE2) in smokers (40).

CONCLUSION:

Fever, cough, dyspnea, and chest pain were the most presenting complain. Haematological changes in COVID 19 patients were "Lymphopenia", "neutrophilia" and "thrombocytopenia". "Neutrophils count" was significantly higher in severe cases in comparison to mild and moderate cases. "Platelets count" was significantly low in patients with low WBC. There was no significant

difference between three groups regarding "D.Dimer", "prothrombin time" (PT), "activated partial thromboplastin time" (APTT). "D.dimer" was significantly high in patients with low Hb. Smokers had a mild course of illness.

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