Long Term clinical feature in a Sample of Iraqi Patients Recovered from COVID-19 in Baghdad 2022

[1]Nidhal Talib Hwaidi **[2]Batool Ali Ghalib Yassin**

[1] FIBMS (family medicine) (corresponding Author)
Al-Doura District, Al-karkh Health Directorate, Baghdad, Iraqi Ministry of Health
Email: nedhaltaleb0@gmail.com

[2]Assistant Professor, FICMS-(Community Medicine)
Department of Family and Community Medicine, College of Medicine, University of Baghdad, Baghdad – Iraq
Email: yassinbat@gmail.com

Abstract

Background: Most people who complain corona viruses' disease fully recover, but current evidence suggests approximately 10–20% of people experience a variety of mid and long-term effects after they recover from their initial illness. Yet the current understanding of causes of post corona viruses' disease condition and why some people are more affected is limited.
Aim of study: To identify the persistent symptoms and signs following corona viruses disease and factors related to these symptoms and signs.
Patients and methods: A cross-sectional study was carried out in four primary health care centers within Al-Doura Health District in Baghdad City-Iraq from first of February to 31st of December, 2022 on a sample of patients with previous corona viruses' disease. The symptoms were classified into early or late according to duration (earlier than or longer than three months).
Results: A total of 442 patients were included in the study. Late respiratory features were observed in 44.8% of corona viruses disease patients, late cardiac features were detected in 19.2% of them and musculoskeletal features were observed in 60% of them. Common late clinical features of corona virus's disease were fatigue (49.3%), weakness (36%), hair loss (32.8%), headache (27.8%), muscle pain (25.6%), mood changes (25.8%), brain fog (24.4%), and dyspnea on walking (22.6%).
Conclusions: Diabetes mellitus, respiratory and cardiac clinical features were significantly higher during early manifestation of the illness whereas the dermatological, neurological and mental clinical features were more likely to persist late after corona viruses' disease recovery.

Keywords: Corona viruses' disease, late symptoms, Baghdad.

Introduction

The Coronavirus disease 2019 (COVID-19) was first reported in December 2019 after an outbreak of pneumonia in Wuhan, China.[1] After the dramatic influx of patients with persistent, debilitating symptoms following acute SARS-CoV-2 (COVID-19) infection, the National Institutes of Health announced an initiative to fully investigate the post-acute squeal of COVID-19 (post-acute COVID-19 syndrome [PACS]). Post-acute COVID-19 syndrome can take many forms, from post–intensive care unit syndrome ([2]) to pulmonary fibrosis secondary to aggressive COVID-19 pneumonia. [(3)] However, PACS (also known as long COVID) is one of the most troubling manifestations of PASC that has been reported to date. It is characterized by persistent symptoms that are still present at least 4 weeks after initial infection and often lasting for several months. [(4)] Despite the highly debilitating nature of PACS, the long-lasting symptoms often occur in the absence of severe acute infection, medically explainable physical symptoms, or preexisting comorbidities. [(5, 6)]

A significant number of patients who have recovered from acute coronavirus disease 2019 (COVID-19) infection are reporting lasting symptoms resulting in impairment of everyday activities beyond the initial acute period. These poste COVID-19 patients suffer from a phenomenon known as ‘long’ or ‘chronic’ COVID-19, or more recently, post-acute squeal of COVID-19 or post-acute COVID-19 Syndrome (PACS). [(7, 8)]

The terms ‘long COVID-19’ and ‘post-acute COVID-19 syndrome’ lack a unified definition. The definition endorsed by the National Institute for Health and Care Excellence (NICE) and the World Health Organization (WHO) is a set of ‘signs and symptoms that emerge during or after an infection consistent with COVID-19, persist for more than 12 weeks, and are not explained by an alternative diagnosis. [(9,10)]

Many experts, including the NICE panel, agreed with subdividing this syndrome into two categories: a posteCOVID-19 subacute phase of ongoing symptoms that lasts 4-12 weeks after the onset of illness, and a chronic-phase or long COVID-19, defined as symptoms and abnormalities that last more than 12 weeks after the onset of illness and are not explained by an alternative diagnosis. [(8, 10)]

The Government of Iraq faced the battle against the COVID-19 spreading with measures including boycott for the gathering places, lockdown, school closure, social distance, and implement mass quarantine to decrease the morbidity rate of COVID-19. [(11)] Ministry of Health in Iraq take action especially for the COVID-19 patients, giving vital free clinical materials and setting up team committee for the COVID–19 to check the people who have been infected with the virus and mandatory quarantine them then start carrying out human trial for coronavirus vaccine. Iraq's authority late lockdown all the states, closure of borders and air terminals after coronavirus cases rise gradually as a feature of the measures to forestall the pandemic COVID-19. [(12)]

A recent retrospective study on 57 patients investigated the impact of COVID-19 on pulmonary function in the early convalescence phase. It collected the data 30 days after discharge and they reported that 54.3% had abnormal CT findings and 75.4% had an abnormal pulmonary function. Compared to the non-severe cases, severe infection cases showed diffusing capacity of the lung for carbon monoxide (DLCO) impairment (75.6% vs. 42.5%). They reported that in more than half of the COVID-19 patients there were an impaired diffusion capacity,

lower muscle strength and lung imaging abnormalities. [13]

A 3-month post-discharge study on critical COVID-19 patients who were admitted to ICU showed that 55% of patients had impaired lung function, exhibiting restrictive patterns, altered DLCO in 65% of patients. [14]

Vascular injury or myocardial injury can occur by a direct viral infection and/or indirectly from immune responses to viral infection. Acute clinical cardiovascular manifestations among hospitalized patients with COVID-19 are ventricular dysfunction, cardiogenic shock, myocardial ischemia/infarction, acute heart failure, cardiac shock, stress cardiomyopathy, arrhythmias, venous thromboembolism and arterial thrombosis. [15] Indirect myocardial injury corresponds to the hypoxia-induced due to hypoxic respiratory failure causing small vessel ischemia microvascular injury and thrombosis. Cardiac injury can be also caused due to the dysfunctional immune response reviewed in detail by Chung et al. [16]

Acute kidney injury (AKI) risks are associated with COVID-19. Nugent et al who studied the longitudinal kidney function post-hospital discharge and compared it in patients with and without SARS-CoV- 2 infection. COVID-19-associated AKI develops more severe AKI, and have greater dialysis requirement after discharge. [17]

Stockman et al [18] followed 74 hospitalized patients and found a high rate of long-term recovery in survivors of COVID-19-associated AKI requiring kidney replacement therapy. Stevens et al [19] concluded that a high rate of renal recovery survivors of COVID-19 is associated with AKI requiring replacement therapy. Study conducted by Prevention of Progressive Renal Insufficiency (PIRP) project, concluded that COVID-19 infection and mortality in chronic non dialysis patients were higher than the general population. [20]

Elevated liver function tests have been reported with abnormal levels of aspartate aminotransferases (AST) and alanine aminotransferase (ALT). [21] Liver injury can also be related to drugs. Most patients with COVID-19 show mild liver damage and return to normal, targeted hepatoprotective therapy is necessary in patients with severe liver injury. [22]

Zhan et al. followed 192 SARS-CoV-2 hospitalized patients. Liver injury was detected in 39% at admission and 69.2% had a liver injury during hospitalization. In case of severe COVID-19 hospitalizations, liver injury was observed in 86% of patients. [23]

COVID-19 was not just age bias but also sex bias towards severe disease. [24] A meta-analysis on more than three million reported global cases conformed that male COVID-19 infected patients had three times the odds of requiring the intensive treatment unit admission and higher odds of death compared to women. [25]

A retrospective study of thyroid function analysis with 50 COVID-19 infected patients has been done in comparison to healthy control. The severity of the COVID-19 infection lowers the thyroid hormone and thyroid-stimulating hormone (TSH) and total triiodothyronine levels. About 53% of the patients had lower TSH. After recovery, there were no significant differences were observed in the thyroid functions TSH, total triiodothyronine, total thyroxin, free triiodothyronine and free thyroxin. [26]
Peripheral nervous system (PNS) manifestations have also been reported including neuropathic pain, skeletal muscle injury, Guillain-Barré syndrome, cranial polyneuritis, neuromuscular junction disorders, neuro-ophthalmological disorders, neurosensory hearing loss and dysautonomia. [27]

Concerns have been raised regarding mental health disorders following COVID-

19. In a study by Garrigues et al [28] after a mean of 110.9 days, loss of memory (34%), concentration disorder (30.8%), sleep disorder (28%) and attention disorder (26.7%) were the most frequent mental health disorders. In a large sample size study in USA, COVID-19 was associated with increased rate of psychiatric disease onset in 14 to 90 days' follow-up especially for anxiety disorders, insomnia and dementia. [29]

Assessing long term symptoms of COVID-19 disease is essential in predicting early complications and preventing health deterioration of patients in addition to design prevention and management strategies of COVID-19 disease. [30]

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Aim of study

To identify the persistent symptoms and signs following COVID-19 disease and factors related to these symptoms and signs

MATERIALS AND METHODS

A cross-sectional study was carried out in four primary health care centers within AL-Doura Health District in Baghdad City-Iraq from 1st of February to 31st of December, 2022.

All patients with previous confirmed COVID-19 disease (positive RT-PCR and/or CT scan diagnosis) were the study population.

Inclusion criteria

1. Age (≥20 years).
2. Confirmed previous COVID-19 infection (positive RT-PCR and/or CT scan diagnosis) according to WHO Guideline.
3. Onset of COVID-19 infection more than three month's duration.

The sample size (442) was calculated with equation of $\{Z_{1-\alpha/2}^2 P (1-P)/d^2\}$ as the P was the prevalence of post-covid-19 syndrome in Baghdad which was (66.7%) in recent Iraqi study [8]. The Z was (1.96) and the d was (0.05). A convenient sample of patients with previous COVID-19 disease presented to four primary health care centers of AL-Doura Health District was selected according to inclusion criteria.

The data were collected directly by the researcher from patients or by phone calling from record and filled in a prepared questionnaire. The questionnaire was designed by the researcher and supervisor depending on previous literatures. [2, 4, 6, 8] The questionnaire included the following:

1. Socio-Demographic characteristics of COVID-19 patients: Age, gender, educational level, body mass index and smoking status.
2. COVID-19 disease characteristics: Duration of COVID-19 infection, SPO_2 level, oxygen need, duration of oxygen need, RCU admission and duration of RCU admission.
3. Clinical co-morbidities of COVID-19 patients: Hypertension, asthma, diabetes mellitus, thyroid disease, cardiac disease, neurological disease, renal disease, liver disease, inflammatory bowel disease and others.
4. Early clinical features of COVID-19 disease (earlier than three months).
5. Late clinical features of COVID-19 disease (longer than three months).

The definition endorsed by the National Institute for Health and Care Excellence (NICE) and the WHO is a set of 'signs and symptoms that emerge during or after an infection consistent with COVID-19, persist for more than 12 weeks, and are not explained by an alternative diagnosis [9, 10]

Ethical considerations

1. Ethical approval was obtained from the Scientific Committee at the Department of Family and Community Medicine and the Iraqi Board for Medical Specializations, Council of Family and Community Medicine.
2. Official agreement was taken from primary health care center authorities.
3. Verbal consent was taken from the patients after explaining the aim of the study and ensuring confidentiality.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 22 was used. Statistical Package for Social Sciences (SPSS) version 22 was used for data entry and analysis. Continuous variables were presented as (mean ± standard deviation (SD) and categorical variables were presented as frequencies and percentages. Multiple contingency tables conducted and appropriate statistical tests performed, Chi square and Fishers exact tests were used for categorical variables. In all statistical analysis, level of significance (p value) set at ≤ 0.05.

RESULTS

Among the 542 patients that were contacted, 442 COVID-19 patients were included in the current study, with a response rate of 81.5%. The mean age of the respondents was 32.8±8.4 years SD, the highest proportion was within 31-40 years followed by 20-30 years and the least was among older than 60 years. Females were more than males (55.7% vs. 44.3%) with a female to male ratio of 1.2:1. Regarding the educational level of COVID-19 patients, more than two thirds (68.8%) were with college education or higher. Measuring the BMI showed that more than two thirds of the patients (67.0%) were either overweight or obese. Current smoking was observed in 15.2% of COVID-19 patients, while ex-smoking was observed in 5.4% of patients (**Table 1**).

Mean duration of COVID-19 disease was 2.3 ± 1weeks SD; 44.3% of COVID-19 patients had duration of two weeks, while 3.2% of them had duration of more than four weeks. The SPO_2 level was not measured in 143 (32.3%) of COVID-19 patients, among the 299 patients with SPO_2 measurement; SPO_2 level was 91-100% in 88.6% of them. Oxygen supply was needed in 2.9% of COVID-19 patients; 61.5% for one week or less and 38.5% for more than one week. RCU admission was needed for four patients only (0.9%) with one-week duration or less (**Table 2**).

The clinical co-morbidity was positive in 139 (31.4%) of COVID-19 patients; hypertension in 59 (13.3%), asthma in 38 (8.6%), thyroid in 24 (5.4%), diabetes mellitus in 23(5.2%), cardiac in 20 (4.5%), and the least was inflammatory bowel diseases in 5 (1.1%) of the patients (**Table3**).

The commonest early clinical features of COVID-19 disease were fever in 358 (81%), dyspnea 358 (81%), weakness in 285 (64.5%), fatigue in 275 (62.2%), and loss smells in 275 (62.2%) (**Table 4**).

Table 1: Demographic characteristics of COVID-19 patients (n=442)

Variable	No.	%
Age (in years)		
20-30 years	132	29.9
31-40 years	170	38.5
41-50 years	77	17.4
51-60 years	39	8.8
>60 years	24	5.4
Gender		
Male	196	44.3
Female	246	55.7
Educational level		
Illiterate and / or read and write	23	5.2
Primary level	26	5.9
Intermediate and Secondary level	89	20.1
College & higher	304	68.8
Body mass index (weight(kg) /Length (m^2)		
Underweight	5	1.1
Normal	141	31.9
Overweight	195	44.1
Obese	101	22.9
Smoking		
Current smoker	67	15.2
Non-smoker	351	79.4
Ex-smoker	24	5.4
Total	442	100.0

Table 2: COVID-19 disease characteristics

Variable	No.	%
Duration of COVID-19 symptoms		
One week	167	37.8
Two weeks	196	44.3
Three weeks	48	10.9
Four weeks	17	3.8
More than four weeks	14	3.2
Total	442	100.0
SPO_2 level (%) (N=299)(less reading measures)		
91-100%	265	88.6
81-90%	26	8.7
Below 80%	8	2.7
Total	299	100.0
Oxygen need		
Yes	13	2.9
No	429	97.1
Total	442	100.0
Duration of oxygen supply (N=13)(through the day unless go to w/c)		
One week or less	8	61.5
More than one week	5	38.5
Total	13	100.0
RCU admission		
Yes	4	0.9
No	438	99.1
Total	442	100.0
RCU admission duration		
One week or less	4	100.0
Total	4	100.0

Table 3: Clinical co-morbidities of COVID-19 patients

Variable	No.	%
Co-morbidity		
Yes	139	31.4
No	303	68.6
Total	442	100.0
Hypertension		
Yes	59	13.3
No	383	86.7
Asthma		
Yes	38	8.6
No	404	91.4
Diabetes mellitus		
Yes	23	5.2
No	419	94.8
Thyroid diseases		
Yes	24	5.4
No	418	94.6
Cardiac diseases		
Yes	20	4.5
No	422	95.5
Neurological diseases		
Yes	9	2.0
No	433	98.0
Renal diseases		
Yes	8	1.8
No	434	98.2
Liver diseases		
Yes	7	1.6
No	435	98.4
Inflammatory bowel diseases		
Yes	5	1.1
No	437	98.9
Others		
Yes	13	2.9
No	429	97.1
Total	442	100.0

Table 4: Early clinical features of COVID-19 disease post 4 weeks

Early features	No.	%
Fever	358	81.0
Dyspnea	358	81.0
Dry cough	154	34.8
Productive cough	136	30.8
Hemoptysis	4	0.9
Rigor	217	49.1
Congestive tonsils	261	59.0
Sneezing	117	26.5
Rhinorrhea	138	31.2
Loss of smells	275	62.2
Loss of taste	236	53.4
Chest pain	85	19.2
Muscle pain	208	47.1
Activity intolerance	99	22.4
Weakness	285	64.5
Joint pain	232	52.5
Fatigue	275	62.2
Palpitation	104	23.5
Dizziness	91	20.6
Headache	225	50.9
Anxiety	108	24.4
Brain fog	64	14.5
Insomnia	90	20.4
Nausea	67	15.2
Vomiting	30	6.8
Diarrhea	93	21.0
Anorexia	138	31.2
Dyspepsia	32	7.2
Abdominal pain	44	10.0
Rash	4	0.9
Menstrual changes	9	2.0
Total	**442**	**100.0**

Regarding systemic early clinical features of COVID-19 disease; **Table 5** showed that general features were observed in 371 (83.9%) of COVID-19 patients, while respiratory features were detected in 412(93.2%), followed by Musculoskeletal complaint in 353(79.9) and Gastrointestinal in 208(47.1%). The least was dermatological features that was found in only 4(0.9%) of the patients.

Table 5: Systemic early clinical features of COVID-19 disease post 4weeks

Variable	No.	%
General features		
Yes	371	83.9
No	71	16.1
Total	442	100.0
Respiratory features		
Yes	412	93.2
No	30	6.8
Total	442	100.0
Cardiac features		
Yes	140	31.7
No	302	68.3
Total	442	100.0
Gastrointestinal features		
Yes	208	47.1
No	234	52.9
Total	442	100.0
Musculoskeletal features		
Yes	353	79.9
No	89	20.1
Total	442	100.0
Neurological & mental features		
Yes	173	39.2
No	268	60.8
Total	442	100.0
Dermatological features		
Yes	4	0.9
No	240	99.1
Total	442	100.0

Common late clinical features of COVID-19 disease were fatigue (49.3%), weakness (36%), hair loss (32.8%), headache (27.8%), muscle pain (25.6%), mood changes (25.8%), brain fog (24.4%), and dyspnea on walking (22.6%) (**Table 6**).

Table 6: Late clinical features of COVID-19 disease post 12 weeks

Late features	**No.**	**%**
Dyspnea on daily activity	84	19.0
Dyspnea on walking	100	22.6
Dry cough	65	14.7
Productive cough	51	11.5
Chest pain	31	7.0
Palpitation	72	16.3
Muscle pain	113	25.6
Weakness	159	36.0
Fatigue	218	49.3
Headache	123	27.8
Brain fog	108	24.4
Anxiety	50	11.3
Mood changes	114	25.8
Insomnia	55	12.4
Rash	3	0.7
Hair loss	145	32.8
Total	**442**	**100.0**

The late respiratory features were observed in 44.8% of COVID-19 patients, while late cardiac features were detected in 19.2% of them and musculoskeletal features were observed in 60% of them (**Table 7**).

Table 7: Systemic late clinical features of COVID-19 disease post 12weeks

Variable	No.	%
Respiratory features		
Yes	198	44.8
No	244	55.2
Total	442	100.0
Cardiac features		
Yes	85	19.2
No	357	80.8
Total	442	100.0
Musculoskeletal features		
Yes	265	60.0
No	177	40.0
Total	442	100.0
Neurological & mental features		
Yes	256	57.9
No	186	42.1
Total	442	100.0
Dermatological features		
Yes	146	33.0
No	296	67.0
Total	442	100.0
Diabetes mellitus		
Yes	5	1.1
No	437	98.9
Total	442	100.0
Menstrual changes		
Yes	17	3.8
No	425	96.2
Total	442	100.0

The respiratory, cardiac and musculoskeletal systemic clinical features were significantly presented earlier in COVID-19 disease (p<0.001). The neurological & mental and dermatological systemic clinical features were significantly presented late in COVID-19 disease (p<0.001). The diabetes mellitus was significantly presented earlier in COVID-19 disease (p=0.002). No significant differences were observed between COVID-19 early and late presentation regarding menstrual changes (p=0.11) **(Table 8**).

Table 8: Distribution of systemic early and late clinical features and chronic disease - COVID-19 diseases

Variable	Onset				P
	Early		Late		
	No.	%	No.	%	
Respiratory features					**<0.001***
Yes	413	67.6	198	32.4	
No	29	10.6	244	89.4	
Cardiac features					**<0.001***
Yes	140	62.2	85	37.8	
No	302	45.8	357	54.2	
Musculoskeletal features					**<0.001***
Yes	353	57.1	265	42.9	
No	89	33.5	177	66.5	
Neurological & mental features					**<0.001***
Yes	173	40.3	256	59.7	
No	268	59.0	186	41.0	
Dermatological features					**<0.001***
Yes	4	2.7	146	97.3	
No	438	59.7	296	40.3	
Menstrual changes					0.11
Yes	9	34.6	17	65.4	
No	433	50.5	425	49.5	
Diabetes mellitus (symptom of DM)					**0.002***
Yes	23	82.1	5	17.9	
No	419	48.9	437	51.1	

***The association was statistically significant (Chi square test, P<0.05)**

There was a highly significant association between positive clinical co-morbidity and late musculoskeletal features of COVID-19 disease (p<0.001). A significant association was observed between positive clinical co-morbidity and late diabetes mellitus accompanying COVID-19 disease (p=0.01). No significant differences were observed between COVID-19 patients with or without clinical co-morbidity regarding respiratory features (p=0.07), cardiac features (p=0.55), neurological & mental features (p=0.07), dermatological features (p=0.5) and menstrual changes (p=0.7) **(Table 9**).

Table 9: Distribution of systemic clinical features and diseases according to COVID-19 clinical co-morbidity.

Variable	Co-morbidity				P
	Yes		No		
	No.	%	No.	%	
Respiratory features					0.07
Yes	71	35.9	127	64.1	
No	68	27.9	176	72.1	
Cardiac features					0.55
Yes	29	34.1	56	65.9	
No	110	30.8	247	69.2	
Musculoskeletal features					**<0.001***
Yes	164	61.9	101	38.1	
No	38	21.5	139	78.5	
Neurological & mental features					0.07
Yes	89	34.8	167	65.2	
No	50	26.9	136	73.1	
Dermatological features					0.5
Yes	43	29.5	103	70.5	
No	96	32.4	200	67.6	
Menstrual changes					0.7
Yes	6	35.3	11	64.7	
No	133	31.3	292	68.7	
Diabetes mellitus					**0.01****
Yes	4	80.0	1	20.0	
No	135	30.9	302	69.1	

** The association was statistically significant (Chi square test, P<0.05)*

***The association was statistically significant (Fishers exact test, P<0.05)*

Discussion

In present study, mean age of COVID-19 patients was 32.8 years with predominance of female gender according to sample. These findings are close to results of Al-Qerem et al [31] cross sectional study in Iraq who found that the majority of COVID-19 patients were less than 40 years' age group with predominance of female gender. Our study found that 68.8% of COVID-19 patients were highly educated. This finding was inconsistent with Maulood et al [32] prospective cross sectional study in Iraq which reported that higher proportion of COVID-19 patients was illiterate. This might be attributed to differences in methodology and selection criteria between two studies. In our study the mean body mass index of COVID-19 patients was 26.8 Kg/m^2 and 22.9% of them were obese. Qasim et al [33] study in Iraq reported that obesity is accompanied with severe COVID-19 disease. Non-smoking was prevalent among studied COVID-19 disease. This finding is consistent with results of Prinelli et al [34] cross sectional study in Italy which found a negative association between current smoking and COVID-19 infection. In this study, mean duration of COVID-19 disease was 2.3 weeks. This finding is close to results of Lane et al [35] retrospective cohort study in United States of America which reported mean duration of COVID-19 disease as (15 days).

Current study showed that clinical co-morbidity was positive in 31.4% of COVID-19 patients; commonly; hypertension, asthma, thyroid, diabetes mellitus and cardiac. These findings are similar to results of Atkins et al [36] study in United Kingdom which reported that about one-third of COVID-19 patients had clinical co-morbidities especially hypertension, diabetes mellitus and asthma.

Common early systemic clinical features of COVID-19 disease recorded in the current study were general features, respiratory features and musculoskeletal features. These findings were close to what was found by Luo et al [37] systematic review study in China, which reported that respiratory symptoms, gastrointestinal features and musculoskeletal features were early systemic clinical features of COVID-19 disease. Our study found that common early clinical features of COVID-19 disease were fever, dyspnea, weakness, fatigue and loss smells (62.2%). These findings were parallel to results of Barzinji et al [38] case series study in Iraq which revealed that common clinical features of COVID-19 disease were fever, headache, dyspnea, weakness, fatigue, and loss smells.

Present study showed that common late systemic clinical features of COVID-19 disease were musculoskeletal features, neurological & mental features, and respiratory features. These findings are in agreement with reports of Nalbandian et al [4] study in United Stated of America which documented that musculoskeletal, neurological, mental and respiratory clinical features were the common late systemic clinical features observed for post-COVID-19 disease. In Iraq, a cross sectional study was conducted by Hassan and Atabatabaee [8] on 165 recovered COVID-19 patients found that musculoskeletal systemic clinical features were the common late COVID-19 systemic features. Another cross sectional study carried out in Iran by Azadvari et al [39] on 239 COVID-19 patients after recovery found that musculoskeletal features were the prevalent features of late COVID-19 disease especially fatigue (91.2%).

Regarding neurological & mental features, Cacciatore et al [40] study in Italy found that cognitive disability, anxiety and hyposmia/hypogeusia represented about one-third of late clinical features of COVID-19 disease that needs early rehabilitation of patients' post-COVID-19 disease. For respiratory system features, Al-Jahdhami et al [41] study sated that after COVID-19 recovery, severe acute infection may develop respiratory complications that might lead to high morbidity and mortality. Our study found that common late clinical features of COVID-19 disease were fatigue, weakness, hair loss, headache, muscle pain and mood changes. These findings were close to results of Raveendran et al [42] from India which revealed that fatigue, cough, chest tightness, breathlessness, palpitations, myalgia and difficulty to focus are symptoms reported in long COVID-19 disease. In Iraq, a cross sectional study conducted by Amen et al [43] on 70 patients after COVID-19 recovery found that most common persistent symptoms recorded were fatigue, dyspnea and chest pain. The discrepancy in frequency of late COVID-19 symptoms is various between different studies in regard to many factors such as age, gender, severity of COVID-19 disease, frequency of early COVID-19 disease and treatment outcomes of the disease.

The present study showed that respiratory, cardiac and musculoskeletal systemic clinical features were significantly presented earlier in COVID-19 disease ($p<0.001$). These findings were similar to results of Hernandez Acosta et al [44] in United States of America which documented that earlier clinical manifestations of COVID-19 disease were respiratory, cardiac and musculoskeletal systemic clinical manifestations. In our study, the neurological & mental and dermatological systemic clinical features were significantly presented late in COVID-19 disease ($p<0.001$). Consistently, Khodeir et al [45] cross sectional study in Egypt on 979 recovered COVID-19 patients found that symptoms related to neurological & mental and dermatological systems were prevalent late clinical manifestations of COVID-19 disease. Our study showed also that diabetes mellitus was significantly presented earlier in COVID-19 disease ($p=0.002$). This finding coincides with results of Gavkare et al [46] review study in India which documented that COVID-19 disease is associated with hyperglycemia and newly incident diabetes mellitus due to many factors such as inflammatory factors, immune mediated factors or direct effect of virus.

The present study found a highly significant association between positive clinical co-morbidity and late musculoskeletal features of COVID-19 disease ($p<0.001$).This finding is parallel to results of Huang et al [47] ambidirectional cohort study in China which reported a significant relationship between pre-existing clinical co-morbidity and late musculoskeletal clinical features of COVID-19 disease. In our study, a significant association was observed between positive clinical co-morbidity and late diabetes mellitus accompanying COVID-19 disease ($p=0.01$).Similarly, Manique et al [48] retrospective study in Portugal on 374 patients with COVID-19 disease reported that pre-existing clinical co-morbidity especially hyperglycemia pre or during COVID-19 disease may have impact on diabetes mellitus late incidence.

Conclusions

- Common late clinical features of COVID-19 disease are fatigue, weakness, hair loss, headache, muscle pain and mood changes.
- The neurological, mental and dermatological clinical features are more likely to persist late after COVID-19 disease recovery.

- The clinical co-morbidities of COVID-19 disease may have impact on developing late clinical features especially musculoskeletal features and diabetes mellitus.

References:

1. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature 2020; 579(7798):265-269.
2. Martillo MA, Dangayach NS, Tabacof L. Postintensive care syndrome in survivors of critical illness related to coronavirus disease 2019: cohort study from a New York City Critical Care Recovery Clinic. Crit Care Med 2021; 49:1427–1438.
3. McGroder CF, Zhang D, Choudhury MA. Pulmonary fibrosis 4 months after COVID-19 is associated with severity of illness and blood leucocyte telomere length. Thorax 2021; 76:1242–1245.
4. Nalbandian A, Sehgal K, Gupta A. Post-acute COVID-19 syndrome. Nat Med 2021; 27:601–615.
5. Davis HE, Assaf GS, McCorkell L. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. medRxiv 2020; 2020.12.24.20248802.
6. Carvalho-Schneider C, Laurent E, Lemaignen A. Follow-up of adults with noncritical COVID-19 two months after symptom onset. Clin Microbiol Infect 2021; 27:258–263.
7. Sandler CX, Wyller VBB, Moss-Morris R, Buchwald D, Crawley E, Hautvast J, et al. Long COVID and Post-infective Fatigue Syndrome: A Review. Open Forum Infect Dis 2021; 8(10):ofab440.
8. Hassan HN, Altabatbaee KSN. Post Covid-19 Syndrome: A Cross Sectional Study in Baghdad. Medico-legal Update 2022; 22 (2): 50-57.
9. World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus. 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1
10. National Institute for Health and Care Excellence (UK). COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020. Available from: https://www.nice.org.uk/guidance/ng188
11. Al-Malkey MK, Al-Sammak MA. Incidence of the COVID-19 in Iraq–implications for travellers. Travel Med Infect Dis 2020; 38: 101739.
12. Ahmad AR, Murad HR. The impact of social media on panic during the COVID-19 pandemic in Iraqi Kurdistan: online questionnaire study. J Med Internet Res 2020; 22: e19556.
13. Huang Y, Tan C, Wu J. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res 2020; 21(1):163.
14. Truffaut L, Demey L, Bruyneel AV. Post-discharge critical COVID-19 lung function related to severity of radiologic lung involvement at admission. Respir Res 2021; 22(1):29.
15. Abrams MP, Wan EY, Waase MP, MorrowJP, DizonJM, Yarmohammadi H, et al. Clinical and cardiac characteristics of COVID-19 mortalities in a diverse New York City cohort. J Cardiovasc Electrophysiol 2020; 31(12):3086-3096.
16. Chung MK, Zidar DA, Bristow MR. COVID-19 and cardiovascular disease: from bench to bedside. Circ Res 2021; 128(8):1214-1236.

17. Nugent J, Aklilu A, Yamamoto Y. Assessment of acute kidney injury and longitudinal kidney function after hospital discharge among patients with and without COVID-19. JAMA Netw Open 2021; 4(3):e211095.
18. Stockmann H, Hardenberg J-HB, Aigner A. High rates of long-term renal recovery in survivors of Coronavirus disease 2019-associated acute kidney injury requiring kidney replacement therapy. Kidney Int 2021; 99(4):1021-1022.
19. Stevens JS, King KL, Robbins-Juarez SY. High rate of renal recovery in survivors of COVID-19 associated acute renal failure requiring renal replacement therapy. PLoS ONE 2020; 15(12):e0244131.
20. Gibertoni D, Reno C, Rucci P. COVID-19 incidence and mortality in non-dialysis chronic kidney disease patients. PLoS ONE 2021; 16(7):e0254525.
21. McGrowder DA, Miller F, Cross MA. Abnormal liver biochemistry tests and acute liver injury in COVID-19 patients: current evidence and potential pathogenesis. Diseases 2021; 9(3):50.
22. Hu LL, Wang WJ, Zhu QJ, Yang L. [Novel coronavirus pneumonia-related liver injury: etiological analysis and treatment strategy]. Zhonghua Gan Zang Bing Za Zhi 2020; 28(2):97-99.
23. Zhan K, Liao S, Li J, Tajiknia V, Zand R, Ghasemi M, Bai Y, Lv L, Yu K, et al. Risk factors in patients with COVID-19 developing severe liver injury during hospitalisation. Gut 2021; 70(3):628-629.
24. Liu C, Mu C, Zhang Q. Effects of infection with SARS-CoV-2 on the male and female reproductive systems: a review. Med Sci Monit 2021; 27: e930168.
25. Peckham H, von Gruijter NM, Raine C. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nat Commun 2020; 11(1):6317.
26. Chen M, Zhou W, Xu W. Thyroid function analysis in 50 patients with COVID-19: a retrospective study. Thyroid 2021; 31(1):8-11.
27. Keyhanian K, Umeton RP, Davoudi BMV. SARS-CoV-2 and nervous system: from pathogenesis to clinical manifestation. J Neuroimmunol 2020; 350:577436.
28. Garrigues E, Janvier P, Kherabi Y. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J Infect 2020; 81(6):e4-e6.
29. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 2021; 8(2):130-140.
30. Koc HC, Xiao J, Liu W, Li Y, Chen G. Long COVID and its Management. Int J Biol Sci 2022; 18(12):4768-4780.
31. Al-Qerem W, Jarab A, Hammad A, Alsajri AH, Al-Hishma SW, Ling J, et al. Knowledge, Attitudes, and Practices of Adult Iraqi Population Towards COVID-19 Booster Dose: A Cross-Sectional Study. Patient Prefer Adherence 2022; 16:1525-1537.
32. Maulood S, Mina M, Ali S. Epidemiological Study of Pandemic COVID-19 and Its Association with Some Chronic Disease in Sulaimani City, Kurdistan Region of Iraq. Kurdistan Journal of Applied Research 2022: 1-8.
33. Qasim AJ, Abbas HM, Jameel RA, Kadhim AF. Obesity and Disease Severity in Iraqi Patients with Covid-19. Nat Volatiles & Essent Oils 2021; 8(6): 2384-2389.
34. Prinelli F, Bianchi F, Drago G, Ruggieri S, Sojic A, Jesuthasan N, et al; EPICOVID19 Working Group. Association between Smoking and SARS-CoV-2 Infection: Cross-sectional Study of the EPICOVID19 Internet-Based Survey.

JMIR Public Health Surveill 2021; 7(4):e27091.
35. Lane A, Hunter K, Lee EL, Hyman D, Bross P, Alabd A, et al. Clinical characteristics and symptom duration among outpatients with COVID-19. Am J Infect Control 2022; 50(4):383-389.
36. Atkins JL, Masoli JAH, Delgado J, Pilling LC, Kuo CL, Kuchel GA, et al. Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort. J Gerontol A Biol Sci Med Sci 2020; 75(11):2224-2230.
37. Luo X, Lv M, Zhang X, Estill J, Yang B, Lei R, et al; COVID-19 evidence and recommendations working group. Clinical manifestations of COVID-19: An overview of 102 systematic reviews with evidence mapping. J Evid Based Med 2022; 15(3):201-215.
38. Barzinji AA, Hamafaraj Jaff H, Ismael SA. Epidemiology and clinical characteristics of patients after recovery from COVID-19 infection in Erbil government, Iraq. Zanco Journal of Medical Sciences (Zanco J Med Sci) 2022; 26(2): 127–136. Available from: https://doi.org/10.15218/zjms.2022.014
39. Azadvari M, Haghparast A, Nakhostin-Ansari A, Emami Razavi SZ, Hosseini M. Musculoskeletal symptoms in patients with long COVID: A cross-sectional study on Iranian patients. Heliyon 2022; 8(8):e10148.
40. Cacciatore M, Raggi A, Pilotto A, Cristillo V, Guastafierro E, Toppo C, et al. Neurological and Mental Health Symptoms Associated with Post-COVID-19 Disability in a Sample of Patients Discharged from a COVID-19 Ward: A Secondary Analysis. Int J Environ Res Public Health 2022; 19(7):4242.
41. Al-Jahdhami I, Al-naamani K, Al-Mawali A, Bennji SM. Respiratory Complications after COVID-19. Oman Med J 2022; 37(1):e343.
42. Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: An overview. Diabetes Metab Syndr 2021; 15(3):869-875. Erratum in: Diabetes Metab Syndr 2022; 16(5):102504. Erratum in: Diabetes Metab Syndr 2022; 16(12):102660.
43. Amen SO, Rasool BQ, Yousif SH, Shakir SS, Shekho BS. The frequency of persistent symptoms after acute COVID19 among Iraqi patients. Med J Babylon 2021; 18:235-240.
44. Hernandez Acosta RA, Esquer Garrigos Z, Marcelin JR, Vijayvargiya P. COVID-19 Pathogenesis and Clinical Manifestations. Infect Dis Clin North Am 2022; 36(2):231-249.
45. Khodeir MM, Shabana HA, Rasheed Z, Alkhamiss AS, Khodeir M, Alkhowailed MS, et al. COVID-19: Post-recovery long-term symptoms among patients in Saudi Arabia. PLoS One 2021; 16(12):e0260259.
46. Gavkare AM, Nanaware N, Rayate AS, Mumbre S, Nagoba BS. COVID-19 associated diabetes mellitus: A review. World J Diabetes 2022; 13(9):729-737.
47. Huang C, Huang L, Wang Y. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. The Lancet 2021; 397(10270):220-232.
48. Manique I, Abegão Matias A, Bouç, B, Rego T, Cortez L, Sabino T, et al. Does the Hyperglycemia Impact on COVID-19 Outcomes Depend upon the Presence of Diabetes?—An Observational Study. Metabolites 2022; 12: 1116. Available from: https://doi.org/10.3390/metabo12111116.