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ORIGINAL PAPER

Prevalence of COVID-19 in Different Types of Vascular Collagen Diseases and its Relationship with Drugs Used in these Patients

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ABSTRACT

Objectives: The outcome of COVID-19 disease in vascular collagen patients and its comparison with other infected people in the community, are not fully understood yet. In this study, we examined whether COVID-19 is more prevalent in these patients, or it is associated with a higher severity of their involvement. **Methods:** This was a retrospective study performed between August and December 2020 on vascular collagen patients referred to the rheumatology clinic of Firouzgar Hospital. Accordingly, the patients were examined for COVID-19. As well, the prevalence of the disease in these patients and its relationship with age, sex, type of disease, medications used, blood type, and history of influenza vaccine were then evaluated. **Results:** Among the total 748 patients, 574 (76.6%) subjects were women, and 174 (23.3%) subjects were men. The mean age of the patients was 47.46 years old; the minimum age was 16 years old, and the maximum age was 82 years old. A total of 60 patients (8%) suffered from COVID-19 and its highest incidence rate was related to rheumatoid arthritis (36.7%) and the lowest one was for vasculitis (1.7%). Notably, 12.5% of the patients who did not suffer from COVID-19, were vaccinated against influenza (p-value = 0.54). In this regard, a significant relationship was found between COVID-19 incidence and previous existence of interstitial lung disease (ILD) (p -value = 0.017). **Conclusions:** The incidence of COVID-19 in vascular collagen patients was not higher than that of the general population and there was no significant relationship among the incidence of COVID-19 and its severity and the type of disease, the drug, and blood group of vascular collagen patients. Since so far, no studies have been performed on the effect of DMARD drugs on the incidence and severity of Covid 19 disease in collagen patients, it seems that if this study can be done with a larger sample size, better results will be obtained.

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INTRODUCTION

Coronaviruses are a large family of viruses that can infect both animals and humans.

A large number of coronaviruses ever known cause many respiratory infections in humans ranged from a common cold to more serious illnesses such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory

Syndrome (SARS).
In some of the studied patients, up-regulation of proinflammatory cells and cytokines consequently caused Cytokines Release Syndrome (CRS) and severe ARDS and symptoms similar to haemophagocytic lymphohistiocytosis (sHLH).[1]
COVID-19 and its associated disease remained unknown until the recent outbreak in Wuhan, China, in December 2019.[2]
One of the concerns with the global spread of the disease in rheumatic patients is that these patients are prone to bacterial and viral infections, because of their autoimmune disease as well as the immunosuppressive drugs that they consume.[3]
A number of drugs used in the treatment of COVID-19 patients and the resulting cytokine storms such as hydroxychloroquine and anti-IL-6 such as Tocilizumab and Colchicine, are known as the drugs used in rheumatic patients.[4]
Therefore, the study aimed to evaluate the prevalence and severity of COVID-19 in these patients by type of vascular collagen disease at first and then to investigate the relationship between the severity of this disease in these patients and antirheumatic drugs used by the patients as well as its relationship with different types of vascular collagen.
In the current research, we also investigated the relationship among the incidence and severity of COVID-19 and influenza vaccine and blood type in patients.

METHODS

This retrospective study was performed on patients referred to the rheumatology clinic of Firoozgar Hospital between August and December 2020.
All the patients diagnosed with rheumatic disease were included in the scheme. Their type of rheumatic disease was firstly recorded, and they were then asked if they were suffering from COVID-19. Thereafter, all patients for whom COVID-19 disease was diagnosed by PCR or ELISA, and a small number due to the typical symptoms of the disease (fever, musculoskeletal pain, sore throat, etc.) and lung CT scan findings (patchy ground-glass change, confluent consolidation, crazy paving, etc.) was diagnosed COVID-19 by physician.
In terms of the severity of COVID-19, if the patient was hospitalised, her/his disease was considered as severe.
We asked all the patients about their history of flu shots in the last year. Afterward, we recorded the patients' blood types and antirheumatic drugs that they were taking. All the obtained data were recorded and analysed in SPSS and p-values were determined using Fisher's Exact test.

RESULTS

Among the total 748 patients, 574 (76.6%) cases were women, and 174 (23.3%) cases were men. The mean age of the patients was 47.46 years old, with the minimum age as 16 years old and the maximum age was 82 years old (**Table 1**).

Table 1. Demographic information.

F/M%	76.6/23.3%
Mean	47.46
Median	46
Std. Deviation	13.56
Minimum	16
Maximum	82

In general, 60 patients (8%) were diagnosed as COVID-19. As well, we were not sure of 5 (0.7%) patients' statuses in terms of coronavirus and 683 (91.3%) patients were resulted as COVID-19.
Of the 60 patients diagnosed with COVID-19, 53 had a positive PCR and 4 had a positive ELISA test, and 3 were diagnosed based on symptoms or CT scan findings.
Among 60 patients with COVID-19, 37 (61.6%) subjects had severe COVID-19 that led to their hospitalization.
Ninety-five (12.8%) patients had a history of influenza vaccine, and 649 (82.8%) patients were not vaccinated.
Out of 60 patients suffering from COVID-19, only 3 (5%) had spondyloarthropathy and 2.5% of all the spondyloarthropathic patients had COVID-19, which was significant with p-value = 0.013.
This indicates a negative association between COVID disease and spondyloarthropathy.
In addition, the relationship between disease type and incidence of COVID-19 in other diseases is given in **Table 3**.

Table 2. Prevalence of any rheumatic disease in the study.

Disease	F/M	Frequency (%)
Rheumatoid arthritis	210/50	34.8%
Spondyloarthropathy	60/63	16.4%
Systemic lupus erythematosus	106/16	16.3%
Scleroderma	84/16	13.4%
Sjögren	37/10	6.3%
Takayasu	30/8	5.1%
Sarcoidosis	15/4	2.5%
Wegener	15/1	2.1%
Behçet's Disease	9/5	1.9%
Myositis	8/0	1.1%

Table 3. Prevalence of COVID-19 infection in patients by type of rheumatic disease.

Disease	In COVID-19+population	In specific rheumatic diseases	In total patient population	P-value
Systemic lupus erythematosus	12/60(20%)	12/122(9.8%)	1.6%	0.46
Spondyloarthropathy	3/60(5%)	3/123(2.43%)	0.4%	0.013
Scleroderma	11/60(18.3%)	11/100(11%)	1.47%	0.23
Rheumatoid arthritis	22/60(36.7%)	22/260(8.46%)	2.94%	0.77
Sjogren	5/60(8.3%)	5/47(10.6%)	0.66%	0.4
Wegener	1/60(1.7%)	1/16(6.3%)	0.13%	0.7
Takayasu	3/60(5%)	3/38(7.9%)	0.40%	0.99
Sarcoidosis	3/60(5%)	3/19(15.8%)	0.40%	0.2

None of the patients with COVID-19 had Behçet's disease and p-value was considered as 0.39.
Out of 60 patients who were infected by coronavirus, only 9 (15%) cases were vaccinated against influenza, and out of 681 patients who did not suffer from coronavirus, only 85 (12.5%) cases were vaccinated against influenza with a p-value of 0.54. In addition, there was no correlation between flu vaccine and not infected by coronavirus.
Table 4 shows the prevalence of drugs used in the studied patients and their relationship with the incidence of COVID-19; as a result, no significant p-value was found.
None of the patients with rheumatoid arthritis received Tocilizumab and the patients with spondyloarthropathy received Secukinumab.
Overall, 85 (11.4%) of the patients in the study had ILD and 60 of these patients had scleroderma (70.6%). (**Table 5**)
Out of 60 patients with COVID-19, 13 (21.7%) patients had ILD and 7(53.8%) of these patients had scleroderma. (**Table 5**)

DISCUSSION

In this study, we investigated the prevalence of COVID-19 in the rheumatic and autoimmune patients referred to our centre (Rheumatology Clinic of Firoozgar Hospital). Moreover, we examined the relationship among the incidence of COVID-19, the type of rheumatic disease, medications used, and the patients' blood type. We asked all the patients about the history of influenza vaccine injection and then examined the relationship between vaccine injection and incidence of COVID-19. Finally, we examined the relationship between pre-existing ILD and the incidence of COVID-19.
Out of 748 patients referred to the clinic, about 8% developed COVID-19 in general.

Table 4. The prevalence of drugs used in the studied patients.

Drug			P-value
Hydroxychloroquine	30/60(50%)	310/742(41.8%)	0.21
Methotrexate	26/60(43.3%)	297/742(40%)	0.58
Sulfasalazine	15/60(25%)	188/742(25.3%)	1
Prednisolone	17/60(28.3%)	137/742(18.5%)	0.4
Rituximab	5/60(8.5%)	25/742(3.4%)	0.4
Infliximab	3/60(5%)	31/742(4.2%)	0.7
Adalimumab	0/0(0%)	17/742(2.3%)	0.3
Etanercept	1/60(1.7%)	24/742(3.2%)	0.7
Cyclophosphamide	2/60(3.3%)	28/742(3.8%)	1
Azathioprine	4/60(6.7%)	69/742(9.3%)	0.64
Leflunomide	2/60(3.3%)	8/742(1.1%)	0.13

Table 5. Prevalence of ILD in patient study with COVID-19 by type of rheumatic disease.

Disease			P-value
Scleroderma	60/85(70.6%)	7/13(53.8%)	0.00
Systemic lupus erythematosus	2/85(2.4%)		0.00
Rheumatoid arthritis	11/85(12.9%)	1/13(7.6%)	0.00
Sjögren	5/85(5.9%)	3/13(23%)	1
Wegener	1/85(1.2%)		1
Sarcoidosis	5/85(5.9%)	2/13(15.3%)	0.05

Table 6. The prevalence of blood groups.

Blood group	Frequency total (%)	Frequency COVID + (%)	P-value
A+	(21.3%) 159	8.9%	0.7
A-	40 (5.4%)	7.7%	1
B+	119(16.1%)	10.6%	0.3
B-	27(3.6%)	3.8%	0.7
AB+	50(6.7%)	10%	0.5
AB-	18(2.4%)	5.6%	1
O+	295(39.8%)	7.8%	0.8
O-	32(4.3%)	3.1%	0.5

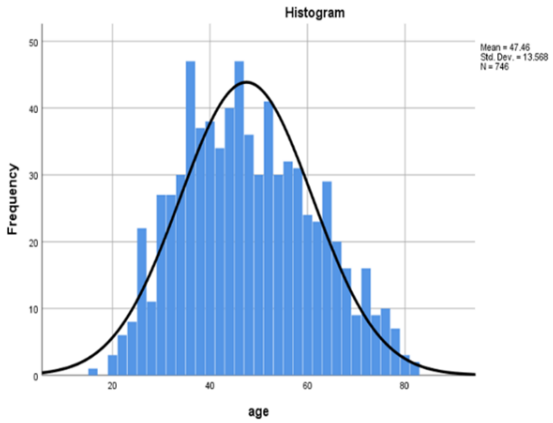

Figure1.

Based on the findings of this study, no direct relationship was observed between the type of vascular collagen disease and the incidence of COVID-19.

We found no significant relationship between influenza vaccine injection and COVID-19 and the p-value was above 0.05.

The most common blood group was O positive, and no significant relationship was found between blood group and coronavirus incidence, which was not significant according to p-value.

In the study by Milena Gianfrancesco et al., which examined the relationship between the hospitalization rate of the rheumatic patients and COVID-19, no correlation was found between the use of rheumatic drugs and the hospitalisation of the patients. Accordingly, this association was significant only with the use of more than 10 mg prednisolone per day.[5]

The 2020 ULAR study by Robert BM Landewé et al. also showed that the prevalence of COVID-19 in rheumatic patients was not higher than that of the general population and there was no need to discontinue these drugs, in order to prevent COVID-19.[6]

In contrast, Silva et al. in their study found that ICU hospitalisation and the need for ventilation were higher in the rheumatic patients than the general population, but the prevalence of the disease and their hospitalisation rates were similar to the general population.[7]

A study by Ennio Giulio Favalli et al. in Italy in 2020 on 123 people with vascular collagen disease showed that the prevalence of COVID-19 was not higher in these patients, so they did not need to discontinue their medication. (8) As well, almost the same result was achieved in our study.

Finally, a study by Fernando Montero et al. in 2020 showed that a specific disease was not associated with a specific vascular collagen disease or DMARD with an increase in hospitalization rate. Correspondingly, only the patients with pulmonary involvement and high dose of steroids briefly had an increase in hospitalisation rate compared to the general population.[9]

In this study, we showed that the prevalence and incidence of COVID-19 in vascular collagen patients were not higher than those of the general population. In addition, there was no significant relationship among the type of disease, drugs used, and blood type of the patients and the incidence and severity of COVID-19 in these rheumatic patients. Only the prevalence and severity of COVID-19 were higher in patients with pre-existing ILD and there was a significant relationship among them (p-value = 0.017).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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