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ORIGINAL ARTICLE

Frequency of the Musculoskeletal Symptoms and Associated Risk Factors among Covid- 19 Patients.

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ABSTRACT

Background: Fatigue, myalgia, and arthralgia are the typical COVID-19 musculoskeletal symptoms, but their prevalence has not been studied extensively. This study was designed to estimate the frequency of different musculoskeletal symptoms among COVID-19 patients and determine the association between the musculoskeletal symptoms and some Sociodemographic characteristics and the severity of the disease.

Methods: A cross-sectional study was conducted among 160 (COVID-19) patients attended screening clinic at Zagazig university hospitals during a period from15-4-2020 to 15-7-2020, they were drown by systemic random method. Clinical assessment was done by taking of sociodemographic data, assessment of the severity of COVID symptoms and assessment of the musculoskeletal through Joint assessment and Fatigue assessment.

Results: The majority of patients developed fatigue and myalgia (60.0%), arthritis, or arthralgia was reported in (47.5%, 45.0%) of patients had back pain. According to Nordic questionnaire, most of studied patients were suffering from musculoskeletal manifestations at neck, lower back, and knee (55.0%, 54.0% and 50.0%) respectively. There was a statistically significant association between arthralgia and sex distribution (p=0.0001) where (61.9%) of females had arthralgia. There was a statistically significant association between myalgia and occupation of the patients (p=0.000) where 82.4% of mentally working patients had myalgia. Binary logistic regression analysis revealed significant models for the prediction of myalgia, fatigue and arthritis/arthralgia.

Conclusions: Musculoskeletal symptoms associated with COVID-19 patients are frequent mostly fatigue and myalgia followed by arthritis or arthralgia, and back pain. Patients with comorbidities were significantly associated with fatigue. Females had arthralgia more than males. Also, a high percent of mentally working patients from urban were complaining of back pain.

Keywords: Musculoskeletal; Frequency; Risk Factors; COVID-19

INTRODUCTION

On March 11, 2020, the novel SARS-CoV-2 (COVID-19) virus was declared by WHO to be a pandemic. Fever, cough, nausea, vomiting, dyspnea, joint pain, weakness, myalgia, headaches, diarrhea, and, in some cases, arthritis are all signs of COVID-19 infection[1]. COVID-19 clinical characteristics range from asymptomatic patients to those suffering from acute respiratory distress syndrome (ARDS) and multiple organ dysfunction[2], [3]. The variety of inflammatory mediators is related to these symptoms. Tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) levels in plasma and upper respiratory secretions are linked to the seriousness of viral replication, fever, and respiratory and systemic symptoms, along with musculoskeletal clinical symptoms[4], [5].

Muscular manifestations in COVID-19 patients vary from myalgia (muscle aches and pain) to myositis and rhabdomyolysis, with a prevalence ranging from 11 to 50 percent [6]. There is a condition known as necrotizing autoimmune myositis. Pathogenesis of muscular involvement in COVID-19 has been studied. The results showed to be affected whether by direct invasion of skeletal muscle by SARS-CoV-2 via the angiotensin-converting enzyme receptors or immune-mediated processes throughout cytokine storming with inflammatory cytokine production and accumulation in skeletal muscles[7].

Coronaviruses are even more frequently associated with arthralgia than clinical arthritis[8]as reported in 2.5%[9]. Some cases of clinical arthritis caused by COVID-19 have been reported, with symptoms resembling reactive or crystalline arthritis. Virus-induced arthritis is distinguished by the onset of arthralgia within a few weeks of viral infection, a self-limiting course, and a good response to nonsteroidal anti-inflammatory drugs (NSAIDs). Serology and synovial fluid testing can help rule out other possible reasons for arthropathy, such as septic arthritis, rheumatoid arthritis, psoriatic arthritis, crystalline arthritis, systemic lupus erythematosus, and reactive arthritis secondary to other infectious diseases[10], [11].

Although these musculoskeletal symptoms are common COVID-19 symptoms, their prevalence has not been widely investigated, so in the current context, we aimed to determine the frequency of different musculoskeletal symptoms among COVID 19 patients and the relationship between musculoskeletal symptoms and sociodemographic characteristics and disease severity.

METHODS

Study design and sampling:

A cross-sectional study that included (COVID-19) patients diagnosed with a positive nucleic acid amplification test and CT chest their ages more than 18 years old. The study included patients attended screening clinic at Zagazig university hospitals during a period of three months (from15-4-2020 to 15-7-2020). The nasopharyngeal swab NAAT had a sensitivity of 84.8% (95% CrI, 76.8%-92.4%) and a specificity of 98.9% (95% CrI, 97.4%-99.8%) [28].After a mean interval of 5 days, a chest CT seems to have 97 percent sensitivity for the diagnosis of COVID-19 pneumonia. Bilateral, peripheral, and basal predominant ground-glass opacities with or without consolidation and bronchovascular thickening are standard chest CT reports in COVID-19 pneumonia. Unusual chest CT discoveries involve central upper lobe dominance, masses, nodules, cavitations, the tree-in-bud sign, lymphadenopathy, and pleural effusion [12].

Using online open epi sample size calculation, by assuming the total numbers of COVID-19 patients attending screening clinic at Zagazig university hospitals during the period of study (three months) in 12000 patients (average attendance numbers per day about 250/4 days per week) and the percentage of myalgia among COVID-19 patients according to Zheng and colleges, 2020 [13]was 12% so the present study sample size will be (160) at 95% confidence level.

Ethical approval was provided by Institutional Review Board of Zagazig University (ZU-IRB# 6418)) according to the Declaration of Helsinki statement of ethical principles published by the World Medical Association (WMA) to guide the protection of human participants in medical research, NO.(ZU-IRB # 6418-20-3-2020). Written informed consent was obtained from all participants.

Suspected and non-confirmed cases, patients less than 18 years and older than 60 years (due to high risk of musculoskeletal pain (MSP) due to osteoporosis osteomalacia), obese patients and those who are suffering from chronic musculoskeletal disorders were excluded from the study.

Clinical assessment:

Sociodemographic data*:* by asking the patients during acute COVID-19 infective stage about their age, residence, occupation and marital status.

The severity of COVID symptoms:

Patients were classified according to the severity of COVID symptoms into asymptomatic, mild, moderate, severe, and critically ill patients according to the National Institutes of Health[14] Asymptomatic patients presented with a positive nucleic acid amplification test for COVID with no symptoms related to COVID-19. Mild type: patients reported any of the different manifestations of COVID-19 (e.g., fever, malaise, headache, muscle pain, cough, sore throat, vomiting, diarrhea, loss of taste and smell) but they do not have pneumonia clinically or by chest imaging. Moderate disease: manifested by pneumonia clinically or by chest imaging with oxygen saturation (SpO2) ≥94% in room air. Severe isoform presented with hypoxemia with SpO2 < 94% and tachypnea > 30 breaths/min. Critically Ill individuals were complicated with respiratory failure, septic shock, and or multiple organ failure.

Assessment of the musculoskeletal involvements*:*

Joint assessment: using the Standardized General Nordic Questionnaire in the literature as a screening tool to quantify the musculoskeletal

pain in 9 body regions[15], administered by the physician.

Fatigue assessment: using Fatigue Assessment Scale (FAS) which is a simple 10-item self-reported questionnaire designed by Michielson et al [16] to assess fatigue in the general population, Five questions reflect physical fatigue and 5 questions (questions 3 and 6-9) mental. Scores on question 4 and 10 should be recoded (1=5, 2=4, 3=3, 4=2, 5=1). The total score ranges from 10 to 50. A total FAS score < 22 indicates no fatigue; a score ≥ 22 indicates fatigue. Also, the patients were asked about myalgia.

Statistical analysis

Statistical analysis was done using SPSS software version 27 (IBM, 2020)27. Data was presented in tables. Quantitative data was presented as mean, median, standard deviation and range. Qualitative data was presented as frequencies and proportions. Shapiro-Wilk test was used to determine the distribution characteristics of variables and variance homogeneity. Pearson's chi squared test, was used to analyze qualitative variables as appropriate. Student's t-test was used to analyze quantitative variables. Binary logistic regression analysis was done to exclude confounding factors. A P-value of <0.05 was accepted as statistically significant.

RESULTS

The studied patient's mean age was 48.3 ± 14.7 years, more than half (52.5%) were females and (47.5%) were males, more than two thirds (72.5%) were urban. (85%) were married, (42.5%) of them were mentally working, only (27.5%) were smokers and (57.5%) of them had comorbidities (hypertension, diabetes mellitus, bronchial asthma, renal and hepatic) (data not tabulated) .

As regard clinical characteristics fever, cough and fatigue were the most frequent recorded symptoms (97%, 77% and 72.5%) respectively and least was chest pain recorded in 10% of patients. (Table, 1) .

Regarding disease severity, a major proportion had mild disease (52.5%) and least had severe disease in (22.5%) (Figure1).

Regarding the frequency of musculoskeletal manifestations in the studied patients, the majority of them (60.0%) developed myalgia and fatigue (Table, 1).

As regard Body mass index (BMI), majority of the studied sample were having normal weight (48.8%) (Table, 1) .

According to Nordic questionnaire, most of studied patients were suffering from pain at neck, lower back, and knees (55.0%, 54.0% and 50.0%) respectively (figure 2).

There was a statistically significant association between myalgia and occupation of the patients (p=0.000) where 82.4% of mentally working patients had myalgia (Table, 2). Patients with comorbidities were significantly associated with fatigue (p=0.0004) (Table, 2) .

There was a statistically significant association between arthralgia and sex distribution (p=0.0001) where (61.9%) of females had arthralgia. Also, there was a significant association between back pain and (Residence & occupation) (p=0.000) where a high percent (61.8%) of mentally working patients from urban (55.2%) were complaining of back pain (Table, 2).

Binary logistic regression analysis revealed significant models for the prediction of myalgia, fatigue and arthritis/arthralgia. Back pain model was not significant. Mental-effort occupation was found to be a risk factor for myalgia in COVI19 patients [OR 95%:7.0 (1.4 – 35.3)]. Presence of comorbidities was found to be a risk factor for fatigue in COVI19 patients [OR 95%:1.25 (1.1 – 40.9)]. Female patients were more vulnerable to arthritis/arthralgia [OR 95%:3.5 (1.9 – 13.0)].

Table (1): Clinical characteristics of the studied patients:

Variables	Study patients (n=160) (%)
Fever	156 (97.5%)
Cough	124 (77.5%)
Fatigue	96 (60.0%)
Sore throat	112 (70.0%)
Myalgia	96 (60.0%)
General bone ache	116 (72.5%)
Dyspnea	80 (50.0%)
Arthritis or arthralgia	76 (47.5%)
Headache	76 (47.5%)
Back pain	72 (45.0%)
Diarrhea	72 (45.0%)
Loss of smell	62 (45.0%)

Variables	Study patients (n=160) (%)
Vomiting,	44 (27.5%)
Constipation	24 (15.0%)
Chestpain	16(10.0%)
Body mass index (BMI) Under weight Normal Overweight	 19(11.9%) 78(48.8%) 63(39.3%)

Table (2): Association between some musculoskeletal disorders and characteristics of the studied patients:

Variables	Fatigue		Arthritis or arthralgia		Myalgia		Back pain	
	Yes (96)	**No (64)**	**Yes (76)**	**No (84)**	**Yes (96)**	**No (64)**	**Yes (72)**	**No (88)**
Age (years): Mean ± SD	50.7 ± 15.1	44.6 ± 13.7	48.4 ± 15.7	48.1 ± 14.1	46.7 ± 13.8	50.6 ± 16.1	45.8 ± 12.0	50.2 ± 16.6
t (P value)	**2.597(0.01*)**		**0.127(0.899)**		**1.59(0.114)**		**1.88(0.062)**	
Sex: Male (n=76) Female (n=84)	40 (52.6%) 56 (66.7%)	36 (47.4%) 28 (33.3%)	24 (31.6%) 52 (61.9%)	52 (68.4%) 32 (38.1%)	44 (57.9%) 52 (61.9%)	32(42.1%) 32 (38.1%)	36 (47.4%) 36 (42.9%)	40 (52.6%) 48 (57.1%)
x^2(P value)	**3.37(0.070)**		**14.71(0.0001**)**		**0.27(0.605)**		**0.328(0.567)**	
Residence: Rural (n=44) Urban (n=116)	24(54.5%) 72(62.1%)	20(45.5) 44(37.9%)	16(36.4%) 60(51.7%)	28(63.6%) 56(48.3%)	23 (52.3%) 73(62.9%)	21(47.7%) 43(37.1%)	8 (18.2%) 64 (55.2%)	36 (81.8%) 52 (44.8%)
x^2 (P value)	**0.752(0.386)**		**3.018(0.08)**		**1.51(0.22)**		**17.636(0.000**)**	
Marital status: Married (n=136) Not married (n=24)	84 (61.8%) 12 (50.0%)	52 (38.2%) 12 (50.0%)	64 (47.1%) 12 (50.0%)	72 (52.9%) 12(50.0%)	80 (58.8%) 16 (66.7%)	56 (41.2%) 8 (33.3%)	60 (44.1%) 12 (50.0%)	76(55.9%) 12 (50.0%)
x^2(P value)	**1.177(0.278)**		**0.07(0.790)**		**0.523(0.470)**		**0.290(0.593)**	
Occupation: Not working (n=60) Mentally (n=68) Physically (n=32)	38 (63.3%) 44(64.7%) 14(43.8%)	22 (36.7%) 24 (35.3%) 18 (56.3%)	28(46.7%) 36(52.9%) 12(37.5%)	32(53.3%) 32(47.1%) 20(62.5%)	24 (40.0%) 56 (82.4%) 16 (50.0%)	36 (60.0%) 12 (17.6%) 16 (50.0%)	12(20.0%) 42(61.8%) 18(56.3%)	48(80.0%) 26(38.2%) 14(43.8%)
x^2 (P value)	**4.43(0.110)**		**2.107(0.347)**		**25.49(0.0000**)**		**24.51(0.000**)**	
Smoker (44) Nonsmoker(116)	24(54.5%) 72(62.1%)	20(45.5) 44(37.9%)	16(36.4%) 60(51.7%)	28(63.6%) 56(48.3%)	23(52.3%) 73(62.9%)	21(47.7%) 43(37.1%)	18(40.9%) 54(46.6%)	**26 (59.1%)** **62(53.4%)**
x^2 (P value)	**0.752(0.386)**		**3.018(0.082)**		**1.51(0.22)**		0.410(0.522)	
Comorbidities: -yes(n=92) -no(68)	66(71.7%) 30(44.1%)	26 (28.3%) 38(55.9%)	48(52.2%) 28(41.2%)	44(47.8%) 40(58.8%)	50 (54.3%) 46(67.6%)	42 (45.7%) 22(32.4%)	40 (43.5%) 32(47.1%)	**52 (56.5%)** **36(52.9%)**
x^2 (P value)	**0.752(0.386)**		**1.896(0.17)**		**2.88(0.90)**		0.203(0.653)	
Severity: Mild (n=84) Moderate (n=40) Severe (n=36)	48 (57.1%) 22 (55.0%) 26 (72.2%)	36 (42.9%) 18(45.0%) 10 (27.8%)	38(45.2%) 17(42.5%) 21(58.3%)	46(54.8%) 23(57.5%) 15(41.7%)	47(56.0%) 23(57.5%) 26(72.2%)	37(44.0%) 17(42.5%) 10(27.8%)	36(42.9%) 17(42.5%) 19(52.8%)	**48(57.1%)** **23(57.5%)** **17(47.2%)**
P value	**2.94(0.223)**		**2.27(0.322)**		**2.92(0.232)**		1.137(0.566	

Variables	Fatigue		Arthritis or arthralgia		Myalgia		Back pain	
Body mass index (BMI) Under weight (19) Normal (78) Overweight (63)	10(52.6%) 42(53.8%) 44(69.8%)	9(47.4%) 36(46.2%) 19(30.2%)	8(42.1%) 35(44.9%) 33(52.4%)	11(57.9%) 43(55.15) 30(47.7%)	11(57.9%) 41(52.6%) 44(69.8%)	8(42.1%) 37(47.4%) 19(30.2%)	12(63.2%) 32(41.0%) 28(44.4%)	**7(36.8%)** **46(59.0%)** **35(55.6%)**
P value	**4.203(0.123)**		**1.04(0.595)**		**4.374(0.113)**		3.04(0.22)	

t **:** student t test x^2: chi squared test. **: highly significant

Table (3): Binary logistic regression analysis ofindependent variables significantly associated with musculoskeletal symptoms:

Variables	B	SE	Wald	Sig.	Odds ratio (95% CI)
Myalgia: Occupation (Mentally)	1.9	0.83	5.5	**0.01(S)**	7.0 (1.4 – 35.3)
Fatigue : Comorbidities	1.4	0.68	4.2	**0.04(S)**	1.25 (1.1 – 40.9)
Arthritis or arthralgia: Sex (Female)	1.3	0.67	3.6	**0.05(S)**	3.5 (1.9 – 13.0)
Back pain: Residence (Urban) Occupation (Mentally)	 1.4 1.5	 0.93 0.83	 2.1 3.5	 0.1 0.06	 3.9 (0.63 – 24.4) 4.7 (0.92 – 23.9)

B: beta coefficient *SE*: standard error *Wald*: the name of the test

Figure (1) distribution of studied sample according to disease severity

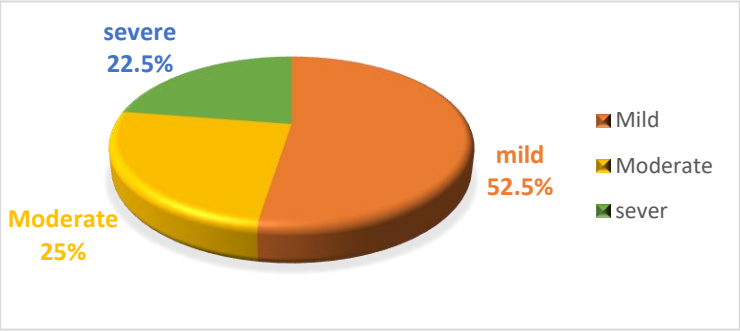
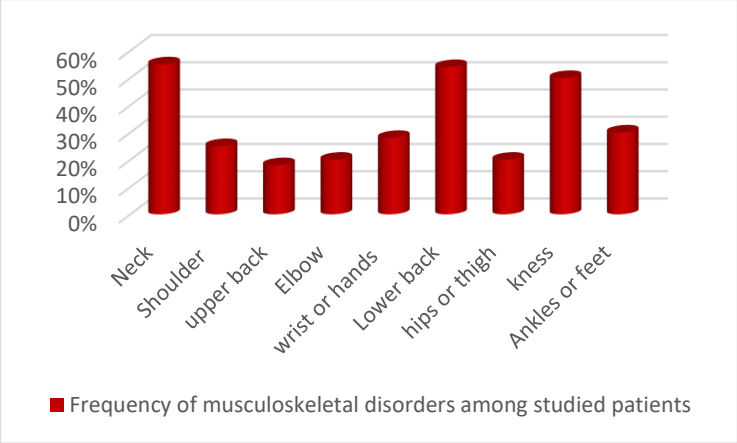


Figure (2): Distribution Frequency of musculoskeletal disorders among studied patients according to Nordic questionnaire.



DISCUSSION

Musculoskeletal disorders were evident in all stages of COVID-19 infection from the outset of the infection up to the end where intensive care unit admitted patients may complain of musculoskeletal manifestations. Fever, dry cough, and fatigue are all common symptoms, as are myalgia and arthralgia[17]. Musculoskeletal symptoms are concerning because they may indicate that inflammatory reactions have overwhelmed the anti-inflammatory effect of NSAIDs, which are widely used by patients[18].

In this study, the patients' mean age was 48.3 ± 14.7 years, there was no significant difference as regard sex distribution where (52.5%) of patients were females and (47.5%) were males, more than two thirds (72.5%) were urban. (85%) and (57.5%) of them had comorbidities (hypertension, diabetes mellitus, bronchial asthma, renal and hepatic). These data are consistent with Cipollaro et al. who reported a slightly higher percentage of females (54%) than males (46%)[19]. Another Chinese study reported less frequency of females and comorbidities of investigated patients as it included 51 males and 48 females and (41%) of patients had comorbidities as hypertension or coronary heart disease were the most common and (6%) had diabetes [13]. Also, Numan[20] found that among the 90 COVID 19 participants, 63 were males and 27 were females with a mean age of 45.43 years. 80 participants were from the urban area.

We recorded that fever was the most common symptom in our patients (97%), followed by cough, fatigue, sore throat, dyspnea, headache, diarrhea, loss of smell, vomiting, constipation and chest pain recorded in (77%, 72.5%,70%, 50%, 47.5%, 45%, 45.0%, 27.5%, 15.0%, 10.0%) respectively. In the Chinese study, a lower frequency of these manifestations was detected in which patients reported fever in 86%, shortness of breath in 35%, gastrointestinal symptoms in 2% with a higher frequency of cough that accounted for 85% of patients [13].

Regarding the frequency of musculoskeletal manifestations in the studied patients, the majority of them (60.0%) developed myalgia and fatigue. Arthritis or arthralgia reported in (47.5%) and (45.0%) of patients had back pain. In agreement with Zhu et al. [3]who reported fatigue in 73% of patients, muscle ache, and headache in 12% of patients. Several studies reported that more than 50% of patients presented with fatigue[21], [22], high frequency of arthralgia/myalgia symptoms[23]. In line with our study, Lechien et al. discovered myalgia in 59% and arthralgia in 31 percent of COVID-19 patients from different European hospitals[24]. According to a study conducted in the United Kingdom, fatigue may continue for some time after the discharge that requires a post-discharge rehabilitation program. This study demonstrated that 72 percent of ICU patients and 60 percent of ward patients expressed exhaustion and breathlessness four to eight weeks after hospital discharge[25]. In contrast to our finding, Cao et al. found a lower prevalence of fatigue symptoms (25.6%), arthralgia and/or myalgia in (15.5%) [17].

In the current study, a major proportion had mild disease (52.5%), moderate disease reported in (25.0%) and severe disease in (22.5%) Our results are confirmed by Numan[20]stated that 66.66% had mild disease , 22.22 % had moderate and 11.12 % had severe disease. Also, Yang et al, who found that fever, fatigue, and a dry cough are the most common symptoms in patients with a mild to moderate clinical presentation of the disease, accompanied by headache, nasal congestion, sore throat, myalgia, and arthralgia[22].

According to Nordic questionnaire, most of studied patients were suffering from pain at neck, lower back, and knees (55.0%, 54.0% and 50.0%) respectively. A similar study conducted in Spanish [26] concluded that 69.86% of patients

complained of neck pain, 13.52% shoulder pain,4.75% elbow pain, 1.66% hip joint pain and 1.84 knee joint pain. In contrast, the majority of patients reported pain in lower limbs in a study done by Numan[20] WHO found that among the 90 COVID 19 participants, 34.45% had pain in the lower limb , 27.77 % complained of pain in the head and neck, 24.45 % in the back and 13.33% in the upper limb.

We assessed the association between the different musculoskeletal manifestations and the characteristics of the studied patients to reveal the impact of the socio-demographical variables on the prevalence of musculoskeletal symptoms of COVID-19 infection and we found that a significant association between myalgia and mentally working patients. Patients with comorbidities were significantly associated with fatigue. Females were more likely to develop arthralgia more than males with a statistically significant association between them. Also, a high percent of mentally working patients from urban were complaining of back pain. We explained this finding as those persons were more prone to psychological distress and musculoskeletal disorders , similarly, Numan[20] who found that a significant association was found between the general health and the severity of COVID, general health and severity of weakness, general health and severity of pain.

Our study has some limitations this study was single centred and lack of imaging as musculoskeletal ultrasound and magnetic resonance imaging.

CONCLUSIONS

Musculoskeletal symptoms associated with COVID-19 patients are frequent mostly fatigue and myalgia followed by arthritis or arthralgia, and back pain. Patients with comorbidities were significantly associated with fatigue. Females had arthralgia more than males. Also, a high percent of mentally working patients from urban were complaining of back pain.

Conflict of interest: None

Financial disclosure: None

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