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Research Article

Investigating the Relationship between Types of Pain and Inflammatory Factors: A Retrospective Cohort

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ABSTRACT

Background: Pain is a recognized complication of COVID-19, and identifying the factors influencing it is crucial for diagnosis. Given the significance of pain assessment in viral patients, this study aimed to determine the relationship between different pain types and inflammatory markers in COVID-19 patients.

Methods: This registered registry study included 2,780 COVID-19 patients hospitalized in Ilam City. Data collection involved using a patient demographic form and a researcher's checklist to assess pain status. Data was primarily gathered by reviewing patient files at referral hospitals admitting COVID-19 cases. If necessary, information was missing from the file, researchers collected supplementary data through clinical examinations and patient interviews. All collected data was then entered into SPSS software, version 16.

Results: The prevalence of pain types was high: back pain in 2,067 patients (77.2%), neck pain in 2,060 (77%), headache in 2,219 (82.9%), and myalgia in 2,419 (90.4%). Results indicated that the ESR level was statistically significantly higher ($P<0.05$) in patients experiencing pain in areas such as the neck, back, and head compared to other patients. Furthermore, a significant relationship was found between CRP status and the status of all types of pain ($P<0.05$).

Conclusion: The findings demonstrate a significant association between the pain condition and the inflammatory factors (ESR and CRP) in COVID-19 patients. Due to COVID-19 being an emerging disease, further research in this area is recommended.

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Introduction

Pain represents the most ubiquitous physical problem patients face, ranking as their most common clinical grievance. Its significant power affects people's quality of life in numerous ways [1-2]. Since pain is frequently viewed as a threat, its constituents—namely intensity, suffering, and discomfort—can activate stress. The official definition from the International Pain Association categorizes pain lasting longer than three months as chronic. Essentially, pain is described as an adverse sensory and emotional experience arising from genuine or potential tissue damage [3-5].

Chronic pain is a major problem, and its management can be difficult. Chronic pain, as a global concern and problem in the field of health, creates many psychological, social, and economic consequences for the individual and the society [6-7]. Pain is influenced by various factors such as life experience, ethnic factors, age, education, gender, etc. The experience of pain can be destructive and will have a negative impact on the patient's performance, including physical and mental performance [8-10]. Chronic pain can have a significant financial burden on the global population [11].

Chronic pain in various dimensions, such as back pain, headache, musculoskeletal pain, and abdominal pain, can exist at a young age [12-14]. Pain management does mean the use of pharmaceutical and non-pharmacological measures to control the patient's pain. In fact, pain management goes beyond pain reduction and includes improving the quality of life and the ability to be employed and productive in order to enjoy life [15-16]. In order to properly manage pain, factors affecting it should be identified. Among the factors affecting pain, we can mention the type of disease. Different diseases, depending on the type of disease, have different effects on the pain status of patients [17].

Pain remains the most frequently reported physical ailment encountered by patients and stands as the most common clinical presentation [18-20]. The Covid-19 disease caused a widespread global health crisis, resulting in a significant psychological, social, and economic burden in the world. This disease disrupts people's physical and mental lives on a wide scale and causes many complications for patients [21].

The COVID-19 virus can cause the death of patients by affecting the vital organs of the body, including the respiratory system, heart, stomach, digestion, and brain [22-23]. The incubation period of this disease is between 1 and 14 days and has symptoms of dry cough, fatigue, fever, diarrhea, abdominal pain, sore throat, nasal congestion, headache, myalgia, phlegm production, hemoptysis, chest pain, and arthralgia [24-26].

Patients with chronic pain, especially patients with viral diseases suffering from pain due to limited mobility and physical activity, access to rehabilitation services and physical therapy, etc., are at greater risk in terms of pain intensity [27]. The pathogenesis of pain in Covid-19 patients is influenced by various factors, the main causes of which are under investigation. There is a relationship between pain and inflammatory factors. So that in acute inflammation, the perception of pain increases and leads to the avoidance of painful stimuli as well as the patient's efforts to relieve pain and heal the damaged tissue [28-29]. Due to the fact that Covid-19 is an emerging disease, for this reason, the inflammatory factors that specifically affect the amount and intensity of pain in these patients may be different from other diseases. For this reason, it is necessary to identify the inflammatory factors affecting the pain of these patients [30-31].

Aim

The overall context culminated in stating the study's aim: to determine the relationship between pain types and inflammatory factors in COVID-19 patients.

Methods

In this study, which is a registered registry, 2780 patients with covid-19 were hospitalized in Ilam City.

The method of data collection was that the researchers visited the referral hospitals admitting patients with Covid-19 and checked the files of these patients. If the information required by the researcher's checklist is available in the patient's file, the researchers complete the tool, and if there are no such items in the patient's file, they collect data, including conducting clinical examinations, interviewing the patient, etc. We're doing it.

The cohort for this study was selected based on stringent inclusion criteria: participants were required to be currently hospitalized, have a confirmed diagnosis of COVID-19 documented upon admission, and have granted explicit consent for hospital admission. Patients were systematically excluded if their case information was likely to be incomplete; specifically, this applied to individuals who were discharged in under 24 hours, those who had passed away, or patients who were transferred elsewhere.

The data collection tool included the patient's demographic profile form and the researcher's checklist for examining the patients' pain status. The demographic information form includes questions about gender (male or female), marriage (with a spouse or without a spouse), history of chronic disease (yes or no), history of hospitalization (yes or no), hospitalization of the patient in the ICU (yes or no), the result of the PCR test (yes or no), and also the mean (SD) of the patient's age.

The checklist made by the researcher included a checklist consisting of two parts to examine the patient's pain condition and the condition of inflammatory factors. Questions about pain include the presence or absence of various types of pain, including pain in the areas (neck, back, headache, and generalized myalgia) and inflammatory factors, including CRP and ESR.

After collecting the data and entering it into SPSS software version 16.

Results

The result showed, regarding the gender of the patients, 1433 (53.6%) of the patients were male and 1243 (46.4%) were female. Regarding the marital status of the patients, 1276 (47.7%) had a spouse and 1276 (47.7%) did not have a spouse. Regarding the history of chronic disease, 2051 (76.6%) had a history of illness, and 625 (23.4%) had no history. They were chronic diseases.

Also, in terms of PCR test status, it was shown that 2553 (95.4%) of positive patients tested and 123 (4.6%) of negative patients tested. On the other hand, regarding the hospitalization status of the patient in the intensive care unit, it was shown that 1897 (70.9%) of the patients were hospitalized in the intensive care unit and 779 (29.1%) were not hospitalized in the said unit.

The study revealed a high prevalence for several types of pain among the patients: back pain was reported by 2067 individuals (77.2%), neck pain by 2060 (77%), headaches by 2219 (82.9%), and myalgia (muscle pain) by 2419 patients (90.4%) (refer to Table 1). Furthermore, a statistically significant relationship was observed between gender and the presence of pain in specific body regions, including the neck and back ($P<0.05$). A comparison of pain status based on pre-existing chronic diseases (Table 2) demonstrated that the prevalence of all pain types was significantly higher in patients with a history of chronic illnesses compared to those without such a history ($P<0.05$).

According to the findings of (Table 3), a significant relationship was observed between the pain condition and the age of the patients. So that as the age of the patients increases, the amount of perceived pain increases. Also, in the examined patients, the number of inflammatory indicators such as ESR and CRP increased with age ($P<0.05$).

The findings of (Table 4) showed that the ESR status of patients with pain in areas such as neck pain, back pain, and headache was higher than other patients, and this level was statistically significant ($p < 0.05$). Also, result showed a relationship between CRP status and the status of all types of pain ($P < 0.05$) (Table5).

Table 1- Comparison of the prevalence of pain in examined patients according to gender

Variable	Male		Female		Total		P, F
	Yes, N (%)	No, N (%)	Yes, N (%)	No, N (%)	Yes, N (%)	No, N (%)	
Neck Pain	1132(79)	301(21)	928(74.7)	315(25.3)	2060(77)	616(23)	0.008, 7.07
Back Pain	1148(80.1)	285(19.9)	919(73.9)	324(26.1)	2067(77.2)	609(22.8)	0.000, 14.5
Headache	1182(82.5)	251(17.5)	1037(83.4)	206(16.6)	2219(82.9)	457(17.1)	0.51, 0.41
Myalgia	1290(90)	143(10)	1129(90.8)	114(9.2)	2419(90.4)	257(9.6)	0.48, 0.50

Table 2- Comparison of the prevalence of pain in examined patients according to chronic disease

Variable	Having a chronic disease		No chronic disease		P, F
	Yes, N (%)	No, N (%)	Yes, N (%)	No, N (%)	
Neck Pain	1806(88.1)	244(11.9)	254(40.6)	371(59.4)	0.000, 788.41
Back Pain	1779(86.8)	271(13.2)	287(45.9)	338(54.1)	0.000, 547.54
Headache	1809(88.2)	241(11.8)	409(65.4)	216(34.6)	0.000, 188.06
Myalgia	1878(91.6)	172(8.4)	540(86.4)	85(13.6)	0.000, 15.04

Table 3- Investigating the relationship between age level with Inflammatory factors and reported pain status

Variable	R	R Square	Adjusted R Square	Sum of Squares	F	P
Neck Pain	0.191	0.036	0.036	484575.038	101.196	0.000
Back Pain	0.246	0.060	0.060	472521.134	171.991	0.000
Headache	0.251	0.063	0.063	471232.402	179.774	0.000
Myalgia	0.068	0.005	0.004	500610.685	12.301	0.000
ESR	0.389	0.151	0.151	426820.661	476.716	0.000
CRP	0.483	0.234	0.233	385437.657	814.997	0.000

Table 4- Investigating the relationship between ESR level and reported pain status

Variable	R	R Square	Adjusted R Square	Sum of Squares	F	P
Neck Pain	0.358	0.128	0.128	40160.380	391.987	0.000
Back Pain	0.239	0.057	0.057	43422.373	161.663	0.000
Headache	0.080	0.006	0.006	45749.902	17.398	0.000

Myalgia	0.001	0.000	0.000	46047.497	0.004	0.949

Table 5- Investigating the relationship between CRP level and reported pain status

Variable	R	R Square	Adjusted R Square	Sum of Squares	F	P
Neck Pain	0.487	0.237	0.237	823.710	831.394	0.000
Back Pain	0.390	0.152	0.152	915.676	479.330	0.000
Headache	0.250	0.062	0.062	1012.505	177.765	0.000
Myalgia	0.113	0.013	0.012	1066.100	34.402	0.000

Discussion

The findings indicated that most COVID-19 patients experienced various types of pain, which aligns with results from similar studies. For instance, a meta-analysis by Gholami et al., which analyzed 33 articles with a total sample size of 3,781 patients, reported prevalences of 10% for headache, 18% for myalgia, 4% for chest pain, and 12% for sore throat among COVID-19 patients [32]. Similarly, a systematic review by Weng et al. showed pain incidence ranges: headache approximately 1.7%-33.9%, abdominal pain 1.9%-14.5%, and myalgia 1.5%-61.0% [33].

Specifically, in the current study, headache was reported in 82.9% of patients. This high prevalence is consistent with the findings of Sampaio et al., who also confirmed the presence of headaches in these patients [34]. However, the prevalence noted in the meta-analysis by Fernández-de-las-Peñas et al. was 47.1% (95% CI 35.8-58.6) [35]. Further supporting the high prevalence seen here, Sampaio et al. also reported that 64.4% of their patients experienced headaches, with 53% reporting severe headaches and 94% reporting bilateral pain [36].

Regarding inflammatory markers, the status of C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR) was found to be elevated in most patients. Specifically, 921 patients (34.4%) had a CRP status of 3+, and 1453 patients (54.3%) were in the 1+ status. The mean (SD) for the ESR inflammatory index was 38.65(±4.14). This contrasts slightly with the ESR M(SD) of 30.99 (±14.77) reported by Purabdollah et al. in Iran [37]. Concerning CRP risk status, Purabdollah et al. found that 50 patients (23.8%) were high-risk, 64 (30.5%) were average-risk, 56(26.7%) were low-risk, and 40 (19%) had normal CRP levels [37].

A significant relationship was observed in this study between CRP status and different types of pain in patients. This finding is supported by Purabdollah et al., who also found an association between pain status and CRP levels (P=0.003) [37]. Moreover, the study by Bilge et al. showed that CRP levels were significantly higher in patients with headaches (mean=12.1) compared to those without (mean=4) (P=0.03) [38], which is consistent with our results.

In broader research examining CRP status in COVID-19 patients, higher CRP levels generally correlate with worse clinical status. Sobhani et al. in Iran reported total CRP levels of 77.73±90.13, with survivors showing 66.80±78.86 and non-survivors showing 100.92±140.94 [39]. However, other studies have shown conflicting results; Sadeghi-Haddad-Zavareh et al. found lower CRP levels in severe patients compared to non-severe ones [37]. This divergence is also seen in other reports where non-severe patients had higher CRP levels than severe ones [40-45]. For example, Chen Tao et al. reported M(SD) CRP for severe patients as 26.2 (8.7-55.2) and for non-severe patients as 113 (69.1-168.4) [40]. Similarly, Zhang Jun et al. found CRP in the severe group to be 7.93 (3.14-22.50) compared to 79.52 (61.25-102.98) in the non-severe group [46].

The severity of COVID-19 and its complications are greater in patients with a history of chronic diseases. In fact, chronic diseases can lead to more harm to the patient due to changes in health status, including faster exposure to infection and severity of the disease [47-50].

Conclusion

Overall, the cited literature suggests that the CRP index is a suitable marker for assessing the clinical condition of COVID-19 patients.

Ethical Approval

The current study was conducted after obtaining approval from the Ethics Committee of Ilam University of Medical Sciences (IR.MEDILAM.REC.1400.103).

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