Assessment of pain in patients with primary immune deficiency

ABSTRACT

**Background:** Primary immune deficiency (PID) patients may develop acute or chronic pain. Pain has not been studied in this population until now.

**Objectives:** This study systematically assessed the pain of various durations in PID patients using validated pain questionnaires.

**Subjects and Methods:** A Short-Form McGill Pain Questionnaire (SF-MPQ), already validated in the Arabic language, was used to ascertain the characteristics and severity of pain. Additionally, an Arabic version of the Neuropathic Pain Questionnaire-Short Form (NPQ-SF) was employed to evaluate neuropathic pain in the same group of patients.

**Results:** Forty-six patients participated in the study. The mean age of the patients was 25 years. The most commonly diagnosed PID was a common variable immune deficiency (32.6%), followed by severe combined immune deficiency (19.57%). Based on the SF-MPQ, the pain was experienced by 30.4% of the subjects who participated in the study; 57% of whom were on regular pain medications. The most common site reported for pain was the abdomen (35.7%). The mean duration of pain was 36.1 days ± 34.6 days. The most common comorbidities in these patients were bronchiectasis, followed by immune thrombocytopenic purpura, and scoliosis. None of the PID patients had significant neuropathic pain based on NPQ-SF.

**Conclusion:** To the best of our knowledge, this is the first study to assess the prevalence as well as the severity and duration of pain in PID patients. There were significantly more subjects who had continuous pain. Treatment of pain in PID patients will have a significant effect on improving their quality of life.

**Key words:** Pain; primary immune deficiency; validated questionnaires

Introduction

Pain is a commonly encountered problem in patients with any chronic illness. Patients with chronic pain may have a suboptimal quality of life.[1] The immune system may play a role in the development of different pain conditions. Although the pain has not been studied in primary immune deficiency (PID), patients with HIV or AIDS have significantly increased pain prevalence.[2,3] Pain is a very distressing symptom; it can be associated with a general feeling of being unwell and a sense of impending doom. Ongoing pain can be a significant issue. Our lack of understanding of...
its mechanisms restricts us in providing effective diagnosis and treatment.

PID disorders result from immune system dysfunction. This can manifest as increased susceptibility to infections. In addition, such disorders can also make a person more prone to allergies, autoimmune diseases, and malignancies. As patients with PID have chronic illnesses, they are prone to acute and chronic pain. Moreover, patients with PID are prone to various infections as well as autoimmune diseases and malignancies. Pain may be one of the earliest presentations in all of the above illnesses, and as such, this symptom should not be ignored as it has diagnostic as well as therapeutic implications.

Furthermore, pain not only affects the quality of life and quality of sleep but also serves as a predisposing factor for other conditions such as anxiety and depression. Patients with PID may present with pain among other symptoms; however, the pain has not been systematically studied in patients with PID, attested to by the paucity or virtual absence of national or international literature on the prevalence of pain in such individuals.

At the immunology clinics at our hospital, PID patients are regularly followed up, and they frequently complain of a variety of pain involving the joints, chest, abdomen, or head.

Patients with PID are more susceptible to developing painful conditions than the general population, possibly because of autoimmune diseases, malignancies, or as part of the PID itself. In addition, opportunistic infections such as herpes simplex or varicella-zoster are painful. Pain, if severe and chronic, can decrease the quality of life and affect psychological functioning. HIV patients also report headaches, joint pain, polyneuropathy, and generalized muscle pain, indicating multiple pain syndromes.

The objectives of the present study were to evaluate the prevalence, severity, duration, chronicity, and intensity of pain in subjects with PID.

The attached pain questionnaire, which reflects neuropathic pain, may contribute to our understanding of pain mechanisms, improve treatment selection, and support a long-range goal of efficient measurement methods that adequately characterize the important domains of pain. Lack of understanding of the underlying etiology may often lead to a delay in appropriate management.

This study is the first step towards understanding pain in patients with PID. The knowledge gained may ultimately help design better ways to predict, diagnose, and treat chronic pain in patients with PID.

Subjects and Methods

This study was approved by the hospital’s Institutional review board (RAC # 2171 054; publication number 2190299). Subjects were recruited from the Immunology Clinics at King Faisal Specialist Hospital and Research Centre, Riyadh, KSA. A waiver of informed consent was obtained from all subjects who participated in the study. Data including medical history, age, gender, ethnicity, and current and past illnesses were collected. The pain was assessed using the Arabic version of the SF-MPQ. Furthermore, a validated Arabic version of the NPQ-SF was also used to assess neuropathic pain in the same group of patients. The original English version of the NPQ-SF can be found here.

The pain treatment history of the patients was documented in addition to other conditions.

All patients aged 14–89 years with any diagnosis of PID, and with the ability to communicate, understand, and answer the questions during the assessment of pain, and who were being followed up in the immunology clinic were enrolled in the study.

Patients who were less than 14 years of age and did not give the waiver of consent to participate in the study or had any obvious cognitive dysfunction were excluded from the study. Women in their menstrual cycles and pregnant women were also excluded.

Statistical analysis

Continuous variables were described as mean ± standard deviation, whereas categorical variables were reported as percentages. Continuous variables were compared using the independent Student’s t-test or ANOVA, while categorical variables were compared using the Chi-square test. The level of significance was set at $P < 0.05$.

Results

A total of 46 patients participated in the study [Table 1]. The mean age was 25 years, and the SD was ± 7.9 years. Males and females were 43.48 and 56.52 %, respectively. The most commonly diagnosed PID was a common variable immune deficiency (32.6%); followed by severe combined immune deficiency (19.7%). Dock 8 mutations were present in 8.7% of the patients. Based on the SF-MPQ, ongoing pain was reported by 30.4% of patients, 57% of whom were
on regular medications for pain. The most common site reported for pain was the abdomen at 35.7%. The mean duration of pain was 36.1 days ± 34.6 days. The most common comorbidities in these patients were bronchiectasis, immune thrombocytopenic purpura, and scoliosis in 21.74%, 6.52%, and 6.52% of patients, respectively. The presence of more than one comorbidity did not increase the chance of developing any type of pain in patients with PID. None of the PID patients had neuropathic pain to any significant degree based on NFQ-SF.

**Discussion**

Chronic pain is a public health concern\(^{[14]}\) that cannot be assessed objectively.\(^{[15]}\) It is difficult to manage pain in patients who may not self-report it.\(^{[16]}\) Significant pain may also be associated with depression.\(^{[17]}\) The SF-MPQ-2 is a validated tool that is increasingly being used to assess pain.\(^{[18]}\)

Although the pain has not been systematically studied in patients with PID, a study of AIDS patients revealed that more than 60% of the patients reported current, frequent, or persistent pain, and many of them had severe pain and dysfunction.\(^{[19]}\)

Even though a number of studies have looked at the quality of life in patients with PID,\(^{[20]}\) there are no previous studies available that assess pain in PID patients, for comparison. However, the pain was reported in 30% of patients with PID in our study, which is quite significant. This was experienced by many different types of PID patients, which means that any patient with PID could be prone to pain and the health care providers should be mindful of it.

Although reported by both males and females, the pain seemed to affect females with a slightly higher frequency. Having one or more comorbidities did not seem to affect the frequency of pain; therefore, patients with any number of comorbidities should be evaluated for pain.

Inefficient pain modulation systems have been reported in other chronic illnesses such as irritable bowel syndrome, fibromyalgia, temporomandibular disorders, and migraines, and have been shown to predict pain postoperatively. Even though the current study itself is not designed to assess pain modulation in patients with PID, it could serve as the basis for studying pain modulation in patients with PID in the future.

In the past years, many efforts have been made for educating and treating patients with AIDS who have chronic pain, thereby improving their quality of life; however, not much work has been done in this regard for patients with PID. The most accepted treatment for chronic pain involves the use of medications, often on a regular basis. These medications can be accompanied by significant side effects. Many trials of different medications have been conducted to select the best-tolerated drug with maximum pain relief. A better understanding of pain in our patients may result in better management of this important symptom as well as their overall well-being.

**Conclusions**

Patients with PID may experience significant ongoing pain. More studies need to be conducted involving a larger number of patients as well as a range of PID patients. Early intervention that leads to the diagnosis of the cause of pain and treatment will have a positive effect on the patients’ quality of life.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Table 1: Patient data**

| Characteristic | Results |
|---------------|---------|
| No. of subjects | 46 |
| Mean age (in years) | 25 ± 7.9 |
| Males: females (%) | 43:57 |
| Commonest primary immune deficiency diagnosis | Common variable immune deficiency |
| Pain (% of patients) | 30 |
| Patients on regular pain meds (% of patients reporting pain) | 57 |
| Commonest site of pain (%) | Abdomen (35.7) |
| Mean duration of pain (days) | 36.1 ± 34.6 |
| Commonest comorbidity (%) | Bronchiectasis 21.74 % |
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Nil.

Conflicts of interest
There are no conflicts of interest.

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### Appendix A

#### Short-Form McGill Pain Questionnaire (SF-MPQ)

| Item | Description                                      | Score |
|------|--------------------------------------------------|-------|
| 1    | Ache throughout your body                        |       |
| 2    | Ache in your limbs                               |       |
| 3    | Ache in your face                                |       |
| 4    | Ache in your head                                |       |
| 5    | Ache in your mouth                               |       |
| 6    | Ache in your throat                              |       |
| 7    | Ache in your ears                                |       |
| 8    | Ache in your eyes                                |       |
| 9    | Ache in your tongue                              |       |
| 10   | Ache in your nose                                |       |
| 11   | Ache in your voice                               |       |
| 12   | Ache in your stomach                             |       |
| 13   | Ache in your abdomen                             |       |
| 14   | Ache in your anus                                |       |
| 15   | Ache in your anus                                |       |
| 16   | Ache in your spine                               |       |

**Rating Scale:**

- **0:** No pain
- **1:** Mild pain
- **2:** Moderate pain
- **3:** Severe pain
- **4:** Very severe pain
- **5:** Worst possible pain

**Visual Analogue Scale (VAS):**

[Graphic representation of a 10 cm line indicating pain intensity from 0 to 10]

From: Ronald Melzack, The short-form McGill Pain Questionnaire, Pain, 30 (1987) 191 – 197.

Terkawi et al. Arabic version of (Short-Form McGill Pain Questionnaire (SF-MPQ)).
Appendix B

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| Appendix B | Terkawi et al. Arabic version of (Neuropathic pain questionnaire-short form (NPQ-SF)) | Page 1 of 1 |

| TOTAL DISCRIMINANT FUNCTION SCORE | | |