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## Pain Perception Model in people with Migraine Headache: The Interplay of Intolerance of Ambiguity and Fear of Disease Progression

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### ABSTRACT

**Purpose:** Migraine headaches are often associated with complex psychological factors that can influence pain perception. This study aims to explore the pain perception model in individuals with migraine headaches, focusing on the role of intolerance of ambiguity and the mediating effect of fear of disease progression.

**Methods and Materials:** A descriptive-correlational design was employed, involving 207 adult participants (aged 30 to 60) diagnosed with migraines in Tehran, 2025. Participants completed validated McGill Pain Questionnaire (MPQ), Ahwaz Migraine Headache Questionnaire (AMQ), Ambiguity Tolerance Scale (ATS), and Short Form of the Fear of Progression Questionnaire (FOP-Q-SF). Statistical analyses were conducted to examine the relationships among these variables. SPSS version 27 software was used to perform descriptive statistics and Spearman correlation, and SmartPLS version 4 software was used to analyze the path between variables.

**Results:** The results indicated that the variable Tolerance of Ambiguity had a significant negative direct effect on Fear of Disease Progression ( $\beta = -0.417$ ,  $p < 0.001$ ). At the same time, the variable Tolerance of Ambiguity also had a significant negative direct effect on Pain Perception ( $\beta = -0.331$ ,  $p < 0.001$ ), leading to a reduction in pain perception. Based on the results, Tolerance of Ambiguity had a significant negative indirect effect on Pain Perception through Fear of Disease Progression ( $\beta = -0.210$ ,  $p < 0.001$ ).

**Conclusion:** These results underscore the intricate relationships between psychological distress, resilience, and pain perception in individuals with migraine headaches. Enhancing resilience may serve as a potential intervention to mitigate the adverse effects of psychological distress on pain experiences.

**Keywords:** Migraine, Pain perception, Psychological distress, Resilience, Intolerance of ambiguity, Fear of disease progression.

## 1. Introduction

Migraine headaches represent a significant public health concern, affecting millions of individuals worldwide. The prevalence of migraines varies across regions, with studies indicating that approximately 10–15% of the population in Iran suffers from this debilitating condition (Haghdooost & Togha, 2022). Comparatively, the global prevalence ranges from 11% to 18%, with variations noted among different demographic groups (Russo & Hay, 2023). These recurrent headaches are characterized by intense pain, often accompanied by nausea, vomiting, and sensitivity to light and sound. Recent research has highlighted the complexity of pain perception in migraine sufferers, suggesting that psychological factors, including intolerance of ambiguity and fear of disease progression, play crucial roles in shaping their experiences (Kaske et al., 2025). Understanding these relationships can inform more effective management strategies for individuals suffering from migraines.

Intolerance of ambiguity refers to an individual's discomfort with uncertainty and ambiguous situations, which can significantly influence emotional and cognitive responses to pain. Studies indicate that individuals with high intolerance of ambiguity may experience heightened pain sensitivity and distress (Guo et al., 2023). This relationship is particularly relevant in the context of migraine, where the unpredictability of attacks can exacerbate psychological distress and lead to a vicious cycle of pain perception and emotional turmoil (Basharpour, 2023). Research has shown that this intolerance can lead to increased anxiety, making it more challenging for individuals to cope with migraine episodes, thus intensifying their overall pain experience (Karimi et al., 2025).

On the other hand, fear of disease progression plays a significant role in the pain perception of individuals suffering from migraines (Kharazi Nutash et al., 2020). Living with recurrent conditions such as migraines creates fears about the future for many patients. They must cope with the complexities and relapses of the disease, increasing functional limitations, disease progression, and a diminished sense of hope (Rogers et al., 2020). It is not unusual for patients with chronic physical illnesses to suffer from fears related to various aspects of their condition. Patients facing a real and ongoing threat do not react in an irrational or inappropriate manner; this type of fear is attributed to fear of disease progression. Consequently, the fear that the disease will worsen is termed fear of disease progression (Sharpe et

al., 2023). Therefore, fear of disease progression is among the most significant stressors for patients with these illnesses. Research has shown that the content related to fear of progression is highly comparable across all studied chronic diseases. However, subtle differences exist regarding the predominant fears in each disease group, suggesting that fear of progression may differ somewhat among various illnesses (Lebel et al., 2020). It is important to distinguish fear of disease progression from the psychiatric concept of anxiety disorders; the primary and common characteristic of neurotic anxiety disorders (such as generalized anxiety disorder, panic disorder, and agoraphobia) is their unrealistic and irrational nature (Curran et al., 2020). In serious illnesses, patients often suffer from real fears related to the disease itself, its treatment, and the associated psychosocial outcomes. Fear of disease progression encompasses a wide range of genuine fears related to the illness and is a normative and appropriate response to the experience of a chronic, debilitating, or potentially fatal condition (Haack et al., 2020). Additionally, fear of disease progression in chronic illnesses, including adults with migraines, may be heightened due to the severity and frequency of headache attacks and their associated complications (Liu et al., 2021).

Studies have shown that fear of progression can be influenced by psychological distress (Momenimovahed et al., 2021) and intolerance of ambiguity (Song et al., 2023), which may exacerbate fear of disease progression in individuals with chronic illnesses. This can have significant negative effects on the mental and physical well-being of those affected by the disease (Sharpe et al., 2023). In summary, the interrelationships among intolerance of ambiguity, fear of disease progression, and psychological distress create a complex framework that significantly influences pain perception in individuals with migraines. Intolerance of ambiguity can lead to increased anxiety and emotional distress, which in turn heightens pain sensitivity and exacerbates migraine symptoms (Guo et al., 2023; Karimi et al., 2025). Concurrently, fear of disease progression contributes to this cycle by amplifying anxiety levels, leading to avoidance behaviors that can worsen the experience of pain (Farris et al., 2025; Haghdooost & Togha, 2022). Psychological distress serves as a mediator in this relationship, with studies showing that higher levels of distress are associated with increased migraine frequency and severity (Ebrahimi et al., 2022; Löwe et al., 2024). This interconnectedness suggests that addressing these psychological factors is essential for effective migraine

management, as they collectively shape the individual's pain experience and overall quality of life (Birkinshaw et al., 2025). By understanding these dynamics, healthcare providers can develop more comprehensive treatment strategies that incorporate psychological support alongside traditional medical interventions.

Despite significant advancements in understanding migraines and the factors influencing them, there remain notable research gaps compared to other studies. Most existing research has focused on the biological and physiological aspects of migraines, with less emphasis on psychological factors such as intolerance of ambiguity and fear of disease progression. This gap in the scientific literature highlights the need for more comprehensive studies that simultaneously examine these psychological factors and their impact on pain perception in individuals with migraines. By integrating these psychological dimensions into the analysis, the research will provide a more holistic understanding of how these factors contribute to the overall migraine experience. This innovative approach is crucial, as it can lead to the development of targeted interventions that address both the physical and psychological aspects of migraine management. By doing so, the study seeks to enhance the existing body of knowledge and inform clinical practices, ultimately improving treatment outcomes for migraine sufferers. This research not only fills a critical gap in the literature but also emphasizes the importance of a biopsychosocial approach in managing chronic pain conditions like migraines. By examining the interplay between intolerance of ambiguity, fear of disease progression, and pain perception, researchers can gain valuable insights into the mechanisms underlying migraine and develop targeted interventions to improve patient outcomes. In conclusion, the interplay of psychological factors such as intolerance of ambiguity and fear of disease progression significantly impacts pain perception in individuals with migraine headaches. As research continues to evolve, it is crucial to integrate these findings into clinical practice to enhance the quality of care for migraine sufferers. By acknowledging the multifaceted nature of pain perception, healthcare providers can better support patients in managing their symptoms and improving their overall well-being.

## 2. Methods and Materials

### 2.1. Study Design and Participants

The present study was a descriptive-correlational design of the structural equation modeling type. The statistical population of this research was selected from adults (aged 30 to 60 years) in Tehran in the year 2025, who experienced migraine headaches. The sampling method was purposive. To determine the sample size, Loehlin (Loehlin, 1992) suggested that for examining a structural model involving 2 to 4 factors, researchers should plan to collect at least 100 to 200 cases. The use of smaller samples could lead to a lack of convergence and result in inappropriate outcomes or low accuracy in parameter estimates, especially concerning standard errors (Hooman, 2008). Therefore, considering this information and the likelihood of some questionnaires being incomplete, a total of 250 questionnaires was designated for the present study.

Participants in this study must have a clinical diagnosis of migraine as defined by the International Classification of Headache Disorders (ICHD) and should be adults aged 30 years and older. Additionally, they must report experiencing psychological distress, which includes symptoms of anxiety and/or depression. All participants are required to provide informed consent to participate in the study and must be willing to complete all assessments and follow-up procedures.

On the other hand, individuals with other primary headache disorders, such as tension-type headache or cluster headache, will be excluded from the study. Those with significant neurological disorders, including epilepsy or multiple sclerosis, will also not be eligible. Furthermore, participants with severe psychiatric conditions, such as schizophrenia or bipolar disorder, that may interfere with their participation will be excluded. Individuals with a history of substance abuse or dependence within the past year will not be included, and pregnant or breastfeeding individuals will also be excluded from the study.

The study followed a systematic and structured approach to ensure the integrity and validity of the research process. Initially, recruitment took place through clinics, hospitals, and online platforms targeting individuals diagnosed with migraines. Interested participants were screened based on the inclusion and exclusion criteria outlined previously.

Once potential participants were identified, they were invited to an initial assessment session where informed consent was obtained. During this session, participants completed a series of questionnaires designed to evaluate

their migraine history, psychological distress (anxiety and depression), and resilience levels. The estimated time for completing the questionnaires was approximately 30 to 45 minutes. These assessments were conducted using validated instruments to ensure reliability and accuracy. Throughout the research process, ethical considerations were strictly adhered to. Participants' confidentiality was maintained, and they were informed about their right to withdraw from the study at any time without penalty. Additionally, the study received approval from an institutional review board (IRB) to ensure compliance with ethical standards.

A total of 250 participants were selected for the study; however, during the research process, 43 individuals were excluded due to incomplete responses or other limitations. Consequently, only 207 questionnaires were included in the analysis.

After data collection, statistical analyses were performed to examine the mediating role of resilience in the relationship between psychological distress and pain perception. The results were interpreted in the context of existing literature, and implications for clinical practice were discussed.

## 2.2. Measures

The McGill Pain Questionnaire (MPQ) is one of the most prominent tools for measuring the sensory and emotional aspects of pain, developed by Melzack (Melzack, 1975). It consists of a total of 20 descriptive items; each rated on a 6-point intensity scale ranging from none (1) to severe (6). In this scale, descriptors 1 to 10 represent the sensory dimension of pain, descriptors 11 to 15 represent the emotional dimension, descriptor 16 represents the evaluative dimension of pain, and descriptors 17 to 20 represent various types of pain. Additionally, the validity and reliability of this questionnaire have been confirmed in Iranian studies, reporting a total Cronbach's alpha of 0.85 and reliability coefficients for all sensory, emotional, and pain intensity evaluation domains above 0.80 (Mousavi & Golmakani, 2018).

The Ahwaz Migraine Headache Questionnaire (AMQ) was designed and developed by Najjarian (Najjarian et al., 1999) to assess migraine headaches in Ahwaz. The questionnaire consists of 25 questions and uses a Likert scale to evaluate migraines with questions such as "Do you fear having a headache in the future when you are not currently experiencing one?" To calculate the total score of the questionnaire, all item scores should be summed. The score

range for this questionnaire is between 25 and 100. A higher score indicates a greater severity of migraine headaches, and vice versa. Validity concerns how well a measurement tool assesses what it intends to measure. In Najjarian's study, the content, face, and criterion-related validity of this questionnaire were deemed appropriate. The reliability of a tool refers to its consistency in measuring what it measures, indicating how consistently it yields the same results under similar conditions (Najjarian et al., 1999). The Cronbach's alpha coefficient for this questionnaire was estimated to be above 0.70.

The Ambiguity Tolerance Scale was developed by McLain (McLain, 2009). This scale is based on revised definitions of ambiguity characteristics and individual reactions to their perceptions. The scale consists of 22 items, and respondents answer using a five-point scale (ranging from "strongly agree" to "strongly disagree"). Scores between 15 and 30 indicate low ambiguity tolerance; scores between 30 and 45 signify moderate ambiguity tolerance, while scores above 45 reflect high ambiguity tolerance. The reliability of the scale has been reported to be above 0.68. Additionally, its correlation with the indecision questionnaire is reported to be 0.57, indicating good construct validity (Hashemi et al., 2017).

The short form of the Fear of Progression Questionnaire, developed by Kwakkenbos et al. (Kwakkenbos et al., 2012), is a self-report questionnaire that consists of 12 items. Respondents answer using a 5-point Likert scale ranging from "never" to "most of the time." The total score is calculated by summing the scores of the subscales, excluding the coping subscale. The minimum score on this questionnaire is 12, while the maximum score is 60, with a score above 34 indicating fear of disease progression. There is no Persian version of this questionnaire available in Iran. However, Khanlari et al. (Khanlari Aziz et al., 2023) translated the questionnaire for use in their study, consulting experts in the field, and reported a Cronbach's alpha of 0.90 for this questionnaire.

## 2.3. Data Analysis

SPSS version 27 software was used to perform descriptive statistics and Spearman correlation, and SmartPLS version 4 software was used to analyze the path between variables. Shapiro-Wilk test was used to examine the normality of the distribution of research variables, and since this test was significant for the research variables, the research variables did not have a normal distribution, so

SmartPLS and the partial least squares method were used. The significance level was considered to be 0.05. The researcher also used the bootstrap method to examine the role of the mediator variable in the model.

### 3. Findings and Results

Table 1 examines the descriptive statistics of the demographic variables of the study. In the gender variable, out of a total of 207 people, 112 (54.1%) were female and 95 (45.9%) were male. In the age variable, people were divided

into three age groups. The age group of 30 to 40 years included 130 people, the age group of 40 to 50 years included 59 people, and the age group of 50 to 60 years included 18 people. The most participants were for the 30 to 40 years group (62.8%). Similarly, the most participants were for the female group (54.1%). In terms of education, people were divided into four main categories including diploma, associate diploma, bachelor's degree, and master's degree. In total, the most participants were for the bachelor's group (35.3%).

**Table 1**

*Description of the demographic variables*

variables	Groups	Frequency	%	N
Gender	Man	95	45.9	207
	Female	112	54.1	
Age	30-40 years	130	62.8	207
	40-50 years	59	28.5	
	50-60 years	18	8.7	
Education	Diploma	53	25.6	207
	Associate Diploma	49	23.7	
	Bachelor's Degree	73	35.3	
	Master's Degree	32	15.5	

Table 2 shows the mean and standard deviation of the research variables.

**Table 2**

*Description of the main research variables*

Variable	N	Mean	SD	Min	Max	Skewness	Kurtosis	Shapiro-Wilk	P-value
Pain perception	207	65.899	11.246	43	89	-0.133	-0.713	0.979	0.004
Fear of disease progression	207	35.343	5.005	21	45	-0.815	0.873	0.923	P<0/001
Tolerance of ambiguity	207	37.087	6.630	28	47	0.007	-1.671	0.862	P<0/001

According to Table 2, the average pain perception was 65.89, the average fear of disease progression was 35.34, and the average tolerance of ambiguity was 37.08. As is clear,

the distribution of the research variables was not normal, because the significance level of the tests was less than 0.05.

**Table 3**

*Spearman's Correlations*

Variable	1	2	3
1. Pain perception	Spearman's rho p-value	— —	— —
2. Fear of disease progression	Spearman's rho p-value	0.651 < .001	*** —
3. Tolerance of ambiguity	Spearman's rho p-value	-0.513 < .001	*** < .001

\* p < .05, \*\* p < .01, \*\*\* p < .001

The pain perception variable had a positive and significant relationship with the Fear of disease progression variable ( $r=0.651, p<0.001$ ). This result shows that with an increase in Fear of disease progression, the level of pain perception also increases. However, the pain perception

variable had a negative and significant relationship with the Tolerance of ambiguity variable ( $r= -0.513, p<0.001$ ). This result shows that with an increase in Tolerance of ambiguity, the level of pain perception also decreases.

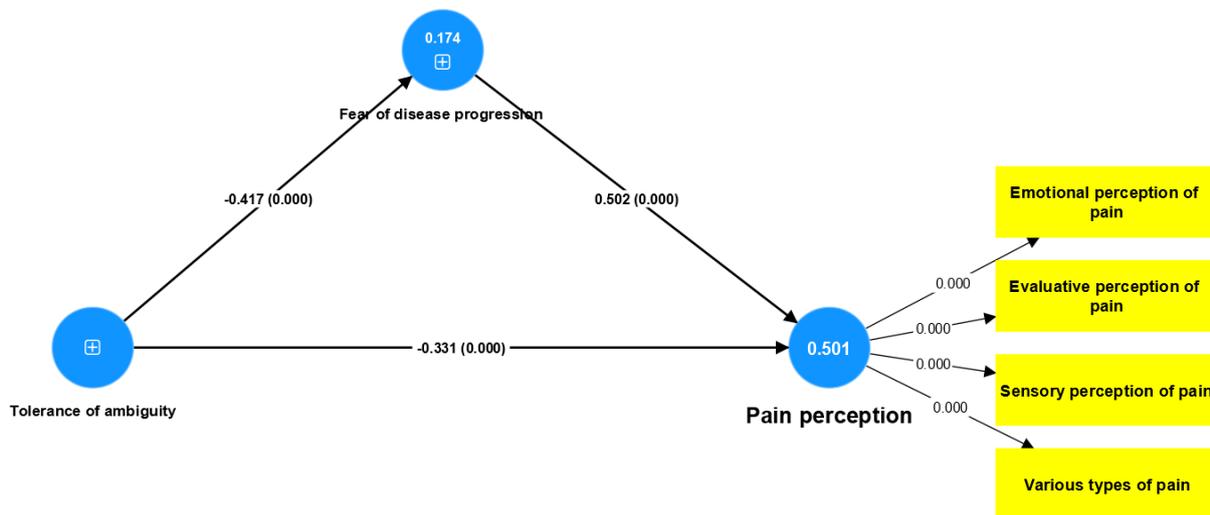
**Table 4**

*Indirect, Direct effects and Total effects*

path coefficient	Estimate	STDEV	t-value	p	95% Confidence Interval		
					2.5%	97.5%	
Direct effects	Fear of disease progression -> Pain perception	0.502	0.060	8.440	$p < 0.001$	0.380	0.613
	Tolerance of ambiguity -> Fear of disease progression	-0.417	0.060	6.917	$p < 0.001$	-0.531	-0.295
	Tolerance of ambiguity -> Pain perception	-0.331	0.053	6.272	$p < 0.001$	-0.438	-0.231
Indirect effects	Tolerance of ambiguity -> Fear of disease progression -> Pain perception	-0.210	0.031	6.669	$p < 0.001$	-0.273	-0.150
Total effects	Tolerance of ambiguity -> Pain perception	-0.540	0.052	10.318	$p < 0.001$	-0.639	-0.434

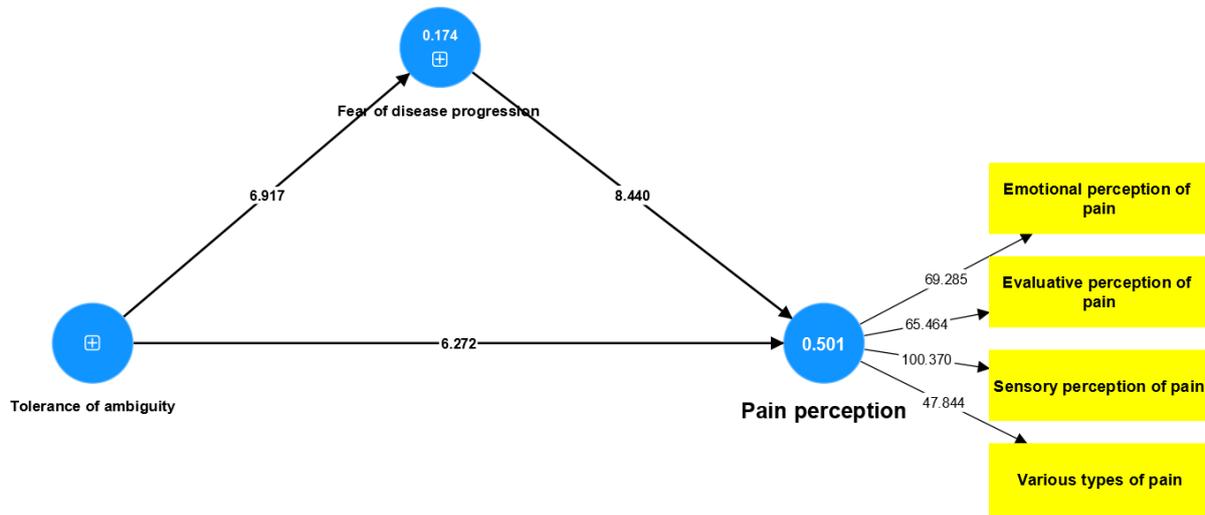
**Figure 1**

*Model with Beta (p) values*



**Figure 2**

*T-values for significance of paths*



Based on the results of Table 4 and Figures 1 and 2, the variable Fear of disease progression had a positive and significant direct effect on Pain perception ( $\beta= 0.502$ ,  $p < 0.001$ ) and caused it to increase. Similarly, the variable Tolerance of ambiguity had a negative and significant direct effect on Fear of disease progression ( $\beta= -0.417$ ,  $p < 0.001$ ) and caused it to decrease. At the same time, the variable Tolerance of ambiguity had a negative and significant direct effect on Pain perception ( $\beta= -0.331$ ,  $p < 0.001$ ) and caused it to decrease. At the same time, in Table 4, the indirect effects were examined. Based on the results, Tolerance of ambiguity had a negative and significant indirect effect on Pain perception ( $\beta= -0.210$ ,  $p < 0.001$ ) through Fear of disease progression. The Sobel test was used to examine the significance of the research mediator variable.

#### 4. Discussion and Conclusion

The primary objective of this study was to investigate the relationships between fear of disease progression and tolerance of ambiguity with the mediating role of pain perception in individuals experiencing chronic pain. Specifically, the study found that fear of disease progression is positively correlated with pain perception, while tolerance of ambiguity negatively influences both fear of disease progression and pain perception. The positive and significant relationship between pain perception and fear of disease progression indicates that as fear of disease progression increases, individuals also report higher levels

of pain perception. This finding is consistent with previous research that suggests heightened anxiety and fear related to health conditions can exacerbate pain experiences (Chen & Wang, 2025; Farris et al., 2025; Huang et al., 2025; Klonowski et al., 2022). For instance, Klonowski et al. (Klonowski et al., 2022) demonstrate that heightened anxiety and depressive symptoms significantly correlate with increased pain sensitivity, suggesting that individuals with migraines may perceive their pain more intensely when experiencing psychological distress.

Similarly, a study by Huang et al. (Huang et al., 2025) found that patients with higher levels of anxiety reported greater pain intensity and frequency of migraine attacks, reinforcing the idea that emotional states can exacerbate pain perception. Moreover, a study by Farris et al. (Farris et al., 2025) found that patients with chronic illnesses who expressed greater fear of their disease reported significantly increased pain levels, suggesting that fear can amplify the subjective experience of pain. Additionally, a study by Haghdoost and Togha (Haghdoost & Togha, 2022) found that fear of disease progression not only correlates with pain intensity but also contributes to the frequency of migraine attacks, suggesting that fear can amplify the subjective experience of pain. Conversely, some studies have indicated that fear may not always correlate with pain perception, such as the research by Filzmoser et al. (Filzmoser et al., 2024), which found no significant relationship between fear and pain intensity in certain populations, highlighting the need for individualized assessments in clinical practice.

Another finding showed the negative and significant relationship between pain perception and tolerance of ambiguity implies that individuals who are more tolerant of ambiguity tend to experience lower levels of pain perception. This finding aligns with research by Song et al. (Song et al., 2023), which indicates that individuals with higher tolerance for uncertainty are better able to manage their pain and cope with chronic health conditions. In contrast, a study by Chen et al. (Chen & Wang, 2025) reported that individuals with low tolerance for ambiguity often experience heightened anxiety and stress, leading to increased pain perception. Therefore, fostering tolerance of ambiguity may provide a beneficial coping mechanism for individuals dealing with chronic pain. The results support the notion that individuals with higher resilience are better equipped to cope with psychological distress, thereby reducing its negative impact on pain perception (Birkinshaw et al., 2025; Ebrahimi et al., 2022). This finding is corroborated by a study which emphasizes that enhancing resilience can significantly improve pain coping strategies in chronic pain patients, including those with migraines (Cosci et al., 2021). In comparison to aligned studies, this research adds depth to the understanding of the psychological dimensions of migraine management. While previous studies have primarily focused on biological and physiological factors, the current findings advocate for a more holistic approach in treatment strategies (Farris et al., 2025; Haghdoost & Togha, 2022). Conversely, studies that have not found significant correlations between psychological factors and pain perception may have overlooked the mediating role of resilience. For example, a study reported no significant association between psychological factors and pain intensity, potentially due to a lack of focus on resilience as a moderating variable. This highlights the necessity for more nuanced research designs that account for these dynamics (Chng et al., 2023).

The direct effects observed in this study further elucidate the intricate relationships among the variables involved. The variable Fear of Disease Progression exhibited a significant positive direct effect on Pain Perception, reinforcing the notion that fear can directly contribute to the experience of pain. This finding aligns with recent studies, such as Basharpour (Basharpour, 2023), which demonstrated that distress intolerance mediates the relationship between fear and pain perception in migraine sufferers. This suggests that heightened fear of disease progression can exacerbate pain experiences, emphasizing the need for interventions that address these psychological factors. Similarly, Tolerance of

Ambiguity demonstrated a negative direct effect on both Fear of Disease Progression and Pain Perception (Basharpour, 2023). These findings support the hypothesis that enhancing tolerance of ambiguity may reduce fear and, consequently, pain perception. This is consistent with the work of Thekkel and Johnson (Thekkel et al., 2025), who found that interventions aimed at increasing tolerance for uncertainty can lead to significant improvements in pain management outcomes. Furthermore, Kharazi Nutash et al. (Kharazi Nutash et al., 2020) highlighted the effectiveness of metacognitive therapy in improving self-efficacy regarding pain and reducing fear of disease progression among individuals suffering from migraine headaches. Their findings underscore the importance of psychological interventions in managing chronic pain conditions.

The relationship between fear, avoidance, and disability in headache disorders has also been explored by Rogers et al. (Rogers et al., 2020), who noted that fear and avoidance behaviors can significantly impact the disability experienced by individuals with headache disorders. This aligns with the current study's findings, suggesting that addressing fear may alleviate pain and enhance overall functioning. Additionally, Zamir et al. (Zamir et al., 2023) conducted a narrative review emphasizing the gaps in headache and migraine treatment, particularly regarding the integration of psychological and behavioral interventions. Their work supports the idea that addressing psychological factors, such as fear and ambiguity tolerance, is crucial in enhancing treatment outcomes for migraine sufferers. The role of fear of progression is further emphasized in the work of Dinkel and Herschbach (Dinkel & Herschbach, 2017), who discussed the implications of fear of progression in cancer patients and survivors, illustrating that fear can significantly affect health outcomes. This perspective is relevant to chronic pain conditions, where fear of disease progression can similarly influence pain perception.

Furthermore, Kaske et al. (Kaske et al., 2025) identified various factors affecting fear of attacks in patients with episodic migraines, highlighting the complexity of these relationships and the need for comprehensive treatment approaches. This fear often arises from concerns about the worsening of symptoms or the potential for chronic pain, leading to increased anxiety and stress (Haghdoost & Togha, 2022). Connery et al. (Connery et al., 2025) also explored associations between death anxiety and fear of illness progression or recurrence, indicating that these fears can have profound effects on individuals' experiences of pain and illness. Lastly, the research by Basha and Smitherman

(Basha & Smitherman, 2025) on the fear of pain in migraines emphasizes the psychological factors influencing perceptions of headache triggers, reinforcing the importance of addressing fear in pain management strategies. Moreover, the indirect effects analysis revealed that tolerance of ambiguity has a negative and significant indirect effect on pain perception through fear of disease progression. This suggests that tolerance of ambiguity may serve as a protective factor against the adverse effects of fear on pain perception. The Sobel test confirmed the significance of this mediating effect, emphasizing the importance of addressing both fear and ambiguity tolerance in therapeutic settings. Previous studies, such as those by Farris et al. (Farris et al., 2025), have similarly highlighted the mediating role of psychological factors in chronic pain, suggesting that interventions targeting these variables could enhance treatment efficacy. However, it is important to note that not all studies agree on the mediating role of tolerance of ambiguity; for instance, a study by Kharkhurin et al. (Kharkhurin et al., 2025) found that while tolerance of ambiguity is beneficial, other factors such as social support may play a more significant role in mediating pain perception. Previous studies, such as those by Löwe et al. (Löwe et al., 2024), have similarly highlighted the mediating role of psychological factors in chronic pain, suggesting that interventions targeting these variables could enhance treatment efficacy.

In conclusion, the findings of this study contribute to the understanding of the psychological dimensions of pain perception. By elucidating the relationships between fear of disease progression, tolerance of ambiguity, and pain perception, the research underscores the need for holistic approaches in pain management that consider both emotional and psychological factors. Future research should continue to explore these relationships and develop interventions that enhance tolerance of ambiguity and reduce fear, ultimately improving outcomes for individuals suffering from chronic pain.

This study faced several limitations that should be acknowledged. Firstly, the sample size may have restricted the generalizability of the findings, as a larger and more diverse population could provide a more comprehensive understanding of the interplay between intolerance of ambiguity, fear of disease progression, and pain perception in individuals with migraine headaches. Secondly, the cross-sectional design limits causal inferences, making it challenging to determine the directionality of the relationships observed. Additionally, self-reported measures

may introduce bias, as participants might underreport or overreport their experiences due to social desirability or lack of awareness. Finally, the study did not account for potential confounding variables such as comorbid psychological conditions, which could influence pain perception and the other variables studied. Future research should aim to include a larger and more diverse sample to enhance the generalizability of the findings. Longitudinal studies are recommended to better understand the causal relationships between intolerance of ambiguity, fear of disease progression, and pain perception over time. Incorporating objective measures alongside self-reports could help mitigate bias and provide a more accurate assessment of participants' experiences. Furthermore, exploring the role of comorbid psychological conditions may offer valuable insights into the complexities of pain perception in individuals with migraine headaches. Finally, interventions designed to enhance resilience and reduce psychological distress could be tested for their effectiveness in improving pain management strategies for this population.

#### **Authors' Contributions**

All authors significantly contributed to this study.

#### **Declaration**

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

#### **Transparency Statement**

Data are available for research purposes upon reasonable request to the corresponding author.

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#### **Declaration of Interest**

The authors report no conflict of interest.

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## Ethical Considerations

In this study, to observe ethical considerations, participants were informed about the goals and importance of the research before the start of the study and participated in the research with informed consent. The study received approval from the Ethics Committee of The Islamic Azad University, Najafabad Branch (IAUN) (Ethical code IR.IAU.NAJAFABAD.REC.1403.181).

## References

- Basha, S., & Smitherman, T. (2025). Fear of Pain in Migraine: Psychological Factors in Perceptions of Headache Triggers. [https://egrove.olemiss.edu/cgi/viewcontent.cgi?article=4352&context=hon\\_thesis](https://egrove.olemiss.edu/cgi/viewcontent.cgi?article=4352&context=hon_thesis)
- Basharpour, S. (2023). Causal Modeling of Pain Perception in Migraine Sufferers Based on Distress Intolerance with the Mediating Role of Fear of Disease Progression: A Descriptive Study. *Journal of Rafsanjan University of Medical Sciences*, 22(9), 929-946. <https://doi.org/10.61186/jrums.22.9.929>
- Birkinshaw, H., de C Williams, A. C., Friedrich, C., Lee, C., Keogh, E., Eccleston, C., & Pincus, T. (2025). Interpersonal Dyadic Influences on Transitions Between Pain States: A Narrative Review and Synthesis. *Pain*, 166(9), 1974-1995. <https://doi.org/10.1097/j.pain.0000000000003544>
- Chen, Y. M., & Wang, J. H. (2025). Cognitive Reserve and Its Associations with Pain, Anxiety, and Depression in Patients with Chronic Migraine: A Retrospective Study. *Journal of clinical medicine*, 14(15), 5193. <https://doi.org/10.3390/jcm14155193>
- Chng, Z., Yeo, J. J., & Joshi, A. (2023). Resilience as a Protective Factor in Face of Pain Symptomatology, Disability and Psychological Outcomes in Adult Chronic Pain Populations: A Scoping Review. *Scandinavian journal of pain*, 23(2), 228-250. <https://doi.org/10.1515/sjpain-2021-0190>
- Connery, T., Riotto, G. D., Macdonald, D., & Menzies, R. E. (2025). Associations Between Death Anxiety and Fear of Illness Progression or Recurrence: A Protocol for a Systematic Review and Meta-Analysis. *PLoS One*, 20(6), e0325176. <https://doi.org/10.1371/journal.pone.0325176>
- Cosci, F., Svicher, A., Mansueto, G., Benemei, S., Chiarugi, A., De Cesaris, F., Guidi, J., & Zipfel, S. (2021). Mental Pain and Pain-Proneness in Patients with Migraine: Results from the PAINMIG Cohort-Study. *CNS Spectrums*, 26(5), 491-500. <https://doi.org/10.1017/S1092852920001480>
- Curran, L., Sharpe, L., MacCann, C., & Butow, P. (2020). Testing a Model of Fear of Cancer Recurrence or Progression: The Central Role of Intrusions, Death Anxiety and Threat Appraisal. *Journal of Behavioral Medicine*, 43, 225-236. <https://doi.org/10.1007/s10865-019-00129-x>
- Dinkel, A., & Herschbach, P. (2017). *Fear of Progression in Cancer Patients and Survivors*. In *Psycho-oncology*. [https://doi.org/10.1007/978-3-319-64310-6\\_2](https://doi.org/10.1007/978-3-319-64310-6_2)
- Ebrahimi, A., Borouni, M., Bagherian-Sararoudi, R., Heidari, Z., & Khorvash, F. (2022). The Role of Mediating the Relationship Between Pain Anxiety and Psychosomatic Components on Quality of Life in Patients with Migraine Headache: Path Analysis. *Journal of Isfahan Medical School*, 39(654), 973-981. [https://jims.mui.ac.ir/article\\_12337.html](https://jims.mui.ac.ir/article_12337.html)
- Farris, S. G., Derby, L., & Kibbey, M. M. (2025). Getting Comfortable with Physical Discomfort: A Scoping Review of Interoceptive Exposure in Physical and Mental Health Conditions. *Psychological bulletin*, 151(2), 131. <https://doi.org/10.1037/bul0000464>
- Filzmoser, N., Webber, I., Kerr, G., Alaa, A., El Asmar, M. I., Karki, M., Riboli-Sasco, E., & El-Osta, A. (2024). Exploring the Link Between Self-Management of Migraine and Emotional Wellbeing: A Cross-Sectional Study of Community-Dwelling Migraine Sufferers. *BMC Neurology*, 24(1), 47. <https://doi.org/10.1186/s12883-024-03535-0>
- Guo, Z., Zhang, W., Lyu, X., Ye, Q., & Peng, W. (2023). Linking Interpretation Bias to Individual Differences in Pain Sensitivity. *Current Psychology*, 42(31), 27472-27484. <https://doi.org/10.1007/s12144-022-03793-6>
- Haack, M., Kramer, S., Seidel, G., & Dierks, M. L. (2020). Quality of Life and Fear of Disease Progression Are Associated with Aspects of Health Literacy in Men with Prostate Cancer from Germany. *Supportive Care in Cancer*, 28, 2283-2292. <https://doi.org/10.1007/s00520-019-05052-0>
- Haghdoust, F., & Togha, M. (2022). Migraine Management: Non-Pharmacological Points for Patients and Health Care Professionals. *Open Medicine*, 17(1), 1869-1882. <https://doi.org/10.1515/med-2022-0598>
- Hashemi, G. S., Sanagoo, A., & Azimi, M. (2017). The Relationship Between Study Habits and Ambiguity Tolerance with Hyperactivity in Graduate Students Azad University of Gorgan. *Development Strategies in Medical Education*, 4(2), 15-26. <http://dsme.hums.ac.ir/article-1-135-fa.html>
- Hooman, K. (2008). A Perturbation Solution for Forced Convection in a Porous-Saturated Duct. *Journal of Computational and Applied Mathematics*, 211(1), 57-66. <https://doi.org/10.1016/j.cam.2006.11.005>
- Huang, B., Chen, W., Peng, C., Wang, Y., Shen, X., Zhang, Q., Yang, L., & Wu, J. (2025). Global Trends in Migraine and Anxiety Over the Past 10 Years: A Bibliometric Analysis. *Frontiers in Neurology*, 15, 1448990. <https://doi.org/10.3389/fneur.2024.1448990>
- Karimi, M. A., Ayatlahi, N., Parachan, P. S., Bigdeli, M., Zeynolabedin, M., & Bayat, M. (2025). Investigating the Relationship Between Tolerance for Ambiguity, Hardiness, and Trauma with Suicidal Tendencies Mediated by Attitudes Toward Death in Young People. *International Journal of New Findings in Health and Educational Sciences (IJHES)*, 3(2), 18-30.
- Kaske, E., Pradela, J., Otto, M., John, L., Derner, N., & Luedtke, K. (2025). Factors Affecting Fear of Attacks in Patients with Episodic Migraine: A Cross-Sectional Study. *Cephalalgia Reports*, 8, 25158163251345140. <https://doi.org/10.1177/25158163251345140>
- Khanlari Aziz, S., Shahgholian, M., & Abdollahi, M. H. (2023). Predicting the Mental Health of Multiple Sclerosis (MS) Patients Based on Relationship Quality, Early Maladaptive Schemas, and Fear of Disease Progression. *Iranian Evolutionary Educational Psychology Journal*, 5(3), 231-244.
- Kharazi Nutash, H., Khademi, A., Babapour, J., & Alivandi Vafa, M. (2020). The Effectiveness of Cognitive-Behavioral Therapy on Signs of Migraine Headaches and Pathological Worry in Female Nurses. *Journal of nursing education*, 8(6), 18-25. <https://jne.ir/article-1-1075-fa.html>
- Kharkhurin, A. V., Koncha, V., & Charkhabi, M. (2025). Effects of Plurilingualism and Pluriculturalism on Creativity: Testing the Mediating Role of Tolerance and Intolerance of Ambiguity. *International Journal of Multilingualism*, 22(2), 475-498. <https://doi.org/10.1080/14790718.2023.2242373>
- Klonowski, T., Kropp, P., Straube, A., & Ruscheweyh, R. (2022). Psychological Factors Associated with Headache Frequency, Intensity, and Headache-Related Disability in Migraine

- Patients. *Neurological Sciences*, 43(2), 1255-1266. <https://doi.org/10.1007/s10072-021-05453-2>
- Kwakkenbos, L., van den Hoogen, F. H., Custers, J., Prins, J., Vonk, M. C., & van Lankveld, W. G. (2012). Validity of the Fear of Progression Questionnaire-Short Form in Patients with Systemic Sclerosis. *Arthritis care & research*, 64(6), 930-934. <https://doi.org/10.1002/acr.21618>
- Lebel, S., Mutsaers, B., Tomei, C., Leclair, C. S., Jones, G., Petricone-Westwood, D., & et al. (2020). Health Anxiety and Illness-Related Fears Across Diverse Chronic Illnesses: A Systematic Review on Conceptualization, Measurement, Prevalence, Course, and Correlates. *PLoS One*, 15(7), e0234124. <https://doi.org/10.1371/journal.pone.0234124>
- Liu, Q., Qin, T., Hu, B., Zhao, Y., & Zhu, X. (2021). Relationship Between Illness Perception, Fear of Progression and Quality of Life in Interstitial Lung Disease Patients: A Cross-Sectional Study. *Journal of clinical nursing*, 30(23-24), 3493-3505. <https://doi.org/10.1111/jocn.15852>
- Loehlin, J. C. (1992). *Genes and Environment in Personality Development*. Sage Publications, Inc. <https://psycnet.apa.org/record/1992-97788-000>
- Löwe, B., Toussaint, A., Rosmalen, J. G., Huang, W. L., Burton, C., Weigel, A., Levenson, J. L., & Henningsen, P. (2024). Persistent Physical Symptoms: Definition, Genesis, and Management. *The lancet*, 403(10444), 2649-2662. [https://doi.org/10.1016/S0140-6736\(24\)00623-8](https://doi.org/10.1016/S0140-6736(24)00623-8)
- McLain, D. L. (2009). Evidence of the Properties of an Ambiguity Tolerance Measure: The Multiple Stimulus Types Ambiguity Tolerance Scale-II (MSTAT-II). *Psychological Reports*, 105(3), 975-988. <https://doi.org/10.2466/PRO.105.3.975-988>
- Melzack, R. (1975). The McGill Pain Questionnaire: Major Properties and Scoring Methods. *Pain*, 1(3), 277-299. [https://doi.org/10.1016/0304-3959\(75\)90044-5](https://doi.org/10.1016/0304-3959(75)90044-5)
- Momenimovahed, Z., Salehiniya, H., Hadavandsiri, F., Allahqoli, L., Günther, V., & Alkatout, I. (2021). Psychological Distress Among Cancer Patients During COVID-19 Pandemic in the World: A Systematic Review. *Frontiers in psychology*, 12, 682154. <https://doi.org/10.3389/fpsyg.2021.682154>
- Mousavi, F. S., & Golmakani, N. (2018). Comparison and Correlation Between Visual Analogue Scale and Different Dimensions of the Short Form of McGill Pain Questionnaire in Post Cesarean Pain Evaluation. *Nursing and Midwifery Journal*, 16(9), 622-630. <https://unmf.umsu.ac.ir/article-1-3611-fa.html>
- Najjarian, B., Attari, Y., & Zargar, Y. (1999). Compilation and Scale Validation for Perfectionism. *Journal of Educational Psychology*, 3(5), 43-58. <https://www.sid.ir/paper/418973/fa>
- Rogers, D. G., Protti, T. A., & Smitherman, T. A. (2020). Fear, Avoidance, and Disability in Headache Disorders. *Current Pain and Headache Reports*, 24, 1-8. <https://doi.org/10.1007/s11916-020-00865-9>
- Russo, A. F., & Hay, D. L. (2023). CGRP Physiology, Pharmacology, and Therapeutic Targets: Migraine and Beyond. *Physiological Reviews*, 103(2), 1565-1644. <https://doi.org/10.1152/physrev.00059.2021>
- Sharpe, L., Michalowski, M., Richmond, B., Menzies, R., & Shaw, J. (2023). Fear of Progression in Chronic Illnesses Other Than Cancer: A Systematic Review and Meta-Analysis of a Transdiagnostic Construct. *Health Psychology Review*, 17(2), 301-320. <https://doi.org/10.1080/17437199.2022.2039744>
- Song, J., Cho, E., Cho, I. K., Lee, D., Kim, J., & Kim, H. (2023). Mediating Effect of Intolerance of Uncertainty and Cancer-Related Dysfunctional Beliefs About Sleep on Psychological Symptoms and Fear of Progression Among Cancer Patients. *Psychiatry Investigation*, 20(10), 912. <https://doi.org/10.30773/pi.2023.0127>
- Thekkel, S. M., Johnson, C. M., Whisenant, M., & Dishman, D. (2025). Pain Acceptance in Chronic Postoperative Pain: Concept Analysis. *Pain Management Nursing*. <https://doi.org/10.1016/j.pmn.2025.01.011>
- Zamir, O., Yarns, B. C., Lagman-Bartolome, A. M., Jobanputra, L., Lawler, V., & Lay, C. (2023). Understanding the Gaps in Headache and Migraine Treatment with Psychological and Behavioral Interventions: A Narrative Review. *Headache: The Journal of Head and Face Pain*, 63(8), 1031-1039. <https://doi.org/10.1111/head.14624>