# Anxiety and Depression in Association with Polypharmacy in Patients with Migraine: A sub-analysis of the PNA One Database - Headache (PNA1DB-Headache)

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#### **ABSTRACT**

#### **Background**

Polypharmacy in patients with chronic disease such as Migraine Headache poses potential harm in patients such that psychological distress may come in. In relation to psychological distress, Migraine Headache patients with multiple drug use are at increased risk of anxiety and depression.

#### **Objectives**

The main objective of the study is to determine the association between anxiety and depression to polypharmacy in migraine headache patients by using the data in the PNA One Headache Database.

#### Methodology

We utilized the data obtained from the Philippine Neurological Association One (PNA-1) Headache Database from 2021 to 2024 and determine the association between Anxiety and Depression to Polypharmacy in patients with Migraine.

#### **Results and Discussion**

The number of medications taken by patients does not significantly differ across depression and anxiety levels, indicating that polypharmacy has no impact on patient's depression and anxiety. However, the study found that patients with anxiety have more tendency to report more severe headache.

#### Conclusion

The study highlights that participants, primarily middle-aged women, experience chronic headaches with high pain severity, often lasting for hours. Educational attainment may influence headache management compliance with a large proportion having only elementary education. Headache onset typically begins in early adulthood, and medication effectiveness often diminishes over time suggesting potential tolerance issues. Anxiety is associated with reporting of increased headache severity while depression does not significantly impact headache characteristics or polypharmacy. The findings emphasize the need for targeted interventions and revised treatment strategies to improve headache management outcomes.

#### Introduction

#### **BACKGROUND**

Chronic illnesses such as migraine headaches pose a challenge in healthcare due to its long-lasting effects and how these diseases impact one's quality of life.<sup>5</sup> Migraines, a debilitating disorder, are often treated with a complex combination of medications resulting in what is known as polypharmacy. Polypharmacy refers to the use of drugs by a patient which is commonly

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seen in individuals dealing with chronic conditions who need both immediate relief and preventive care.<sup>7</sup> While polypharmacy may be necessary for managing the illness it also raises concerns about negative side effects, including emotional strain.<sup>1</sup>

#### Polypharmacy and Chronic Disease Management

The treatment of migraines typically requires a mix of medications such as pain relievers, triptans, antiepileptic drugs, antidepressants and other medications designed to lessen the occurrence and intensity of episodes. While using medications is necessary to tackle the aspects of Chronic Migraine it adds complexity to treatment plans. Each new medication can potentially interact with others, increasing the chances of side effects, drug interactions and placing a burden on the patient.<sup>5</sup> In this study, the chronicity of the Migraine is determined by the Frequency of the Migraine in the data set. Chronic Migraine is defined as having a Migraine episode of 15 or more occurrences in the last three months.

#### **Psychological Distress and Polypharmacy**

Emotional turmoil, including feelings of anxiety, sadness, and tension is what defines distress. The connection between taking medications (polypharmacy) and psychological distress, in individuals dealing with long-term illnesses is becoming an issue. <sup>12</sup> Juggling medications can add to the pressure which possibly worsens the patients' overall well being. For people struggling with migraines this emotional strain is further compounded by the pain and limitations caused by their main health concern. <sup>5</sup>

Several factors contribute to this phenomenon:

1. Medication Side Effects:
Polypharmacy increases the risk of adverse drug reactions, which can include cognitive impairments, mood disturbances, and other psychological symptoms. 16 These side effects can

- directly impact a patient's mental health and quality of life.
- 2. Cognitive Load: Managing multiple medications often requires rigorous adherence to complex dosing schedules, which can create cognitive overload and contribute to stress and anxiety. The fear of medication errors or missed doses can further exacerbate psychological distress.
- 3. Chronic Pain and Disability:
  Migraine itself is associated with significant psychological impact due to its chronic nature, which includes episodes of severe pain, disability, and disruption of daily activities. 18 The additional burden of managing multiple medications may intensify this impact.
- 4. Medication Beliefs and Adherence: The experience of taking numerous medications can influence patients' beliefs about their treatment, potentially leading to feelings of frustration or helplessness. Adherence to medication regimens may be compromised, further complicating disease management and psychological well-being.<sup>11</sup>

A thorough comprehension of the connection between polypharmacy and psychological distress in chronic migraine patients is pivotal to improving treatment outcomes and patient care. This research intends to highlight how polypharmacy influences psychological distress experienced by individuals with chronic migraine and provide a way forward. The goal of this study is to identify clinical practices that can inform intervention processes for both pharmacological and psychological treatments, thus enhancing the overall quality of life and treatment adherence among patients.

It is important to look into the broader implications of such treatment approaches as prevalence of chronic migraines keeps increasing while there is increased use of polypharmacy. The attention directed towards the psychological toll on patients suffering from chronic migraine who are under polypharmacy will contribute towards better holistic management strategies, thereby leading to improved patient results and health state.

Polypharmacy in patients with chronic diseases such as Migraine poses potential harm in patients such that psychological distress may come in. In relation to psychological distress, Migraine patients with multiple drug use are at increased risk of depression. With this, this study aims to determine the association between anxiety and polypharmacy in migraine patients.

### Philippine Neurological Association One Database - Anxiety and Depression Scale

The Philippine Neurological Associated One Database - Headache (PNAOne Database - Headache) utilized the Hospital Anxiety and Depression (HADS) scale. The HADS scale is a validated questionnaire that measures a patient's level of Anxiety and Depression. It provides a total of 21 points which categorizes patients into Normal (0-7), Borderline (8-10) and Abnormal (11-21). This questionnaire has been incorporated in the PNAOne Database - Headache to determine the category of the patients' case of Anxiety and Depression. The result of each patient will then be utilized in this study.

#### **OBJECTIVES**

The main objective of this study is to determine the relationship between polypharmacy and psychological distress in terms of anxiety by using the data in the PNA One Headache Database. Specifically, the study will:

 Determine patients who were diagnosed with migraine in the PNA1 Headache Database;

- 2. Determine the demographics of the respondents in terms of age, sex, educational level, age of onset of first headache;
- 3. Determine the characteristics of Migraine respondents in terms of frequency, duration and severity of the headache;
- 4. Determine the effectiveness of the medication/s taken by the respondents;
- 5. Determine the respondent's category in terms of Polypharmacy (simultaneous use of five or more medications) or Non-Polypharmacy;
- 6. Determine the Anxiety Score of patients with Migraine;
- 7. Determine the Depression Score of patients with Migraine; and
- 8. Determine if there is an association between Polypharmacy and Anxiety score and Depression score in patients with Migraine in terms of demographics, characteristics of headache and effectiveness of medications.

#### **SIGNIFICANCE**

The significance of the study are as follows:

- Provide insight in the association of Polypharmacy and Level of Anxiety in patients with Migraine;
- 2. Aid the physicians in the management and streamlining of multiple medications in patients with Migraine; and
- 3. Increase awareness patients with regards to their understanding of the possible association of polypharmacy and anxiety

#### **TECHNICAL DEFINITION OF TERMS**

**Anxiety** - The level of anxiety of each patient were determined by their score concurred from the Hospital Anxiety and Depression (HADS) Scale as follows: Normal (0-7), Borderline (8-10) or Abnormal (11-21).

**Depression** - Patients were categorized into Normal (0-7), Borderline (8-10) or Abnormal (11-21) as per HADS scale.

**Duration** - Duration were presented as Seconds / Minutes / Hours / Days / Daily as seen in the PNA One Headache Database.

Effectiveness - The effectiveness were categorized as reflected in the PNA One Headache Database as follows: Effective; Initially effective but later not that effective; Definitely not effective; and Effective but with side effects; this is treated as a categorical data.

**Frequency** - Frequency pertains to the number of headaches *per day, per week,* or *per month* as can be seen in the PNA One Headache Database. This is treated as a categorical type of data.

**Polypharmacy** - prescribed for the migraine headache of more than one medications). <sup>13,17</sup> In the context of this study, the medications taken for Polypharmacy is defined with the medication taken either singly at a point in time and/or together.

**Severity** - Severity was presented as a categorical type of data entry as follows: *No pain; Little bit pain; Little more pain; Even more pain; Much more pain; or Worst pain* as reflected in the PNA One headache Database.

#### Study Design

#### **METHODOLOGY**

This retrospective study utilized the data from the Philippine Neurological Association One Database - Headache which

is a multi-center collection of data involving all the accredited neurology training institutions in the Philippines.

#### **Patient's Eligibility**

Patients who are already enrolled in the PNA One Database -Headache from 2021 to 2024.

**Inclusion Criteria:** All patients records that are enrolled in the PNA One Database - Headache.

**Exclusion Criteria:** Patient records which are incomplete in data.

#### **Data Collection**

The proposal was submitted to the Steering Committee of the Philippine Neurological Association One Database -Headache (PNA1DB Headache). The was approved and subsequent submission to the Makati Medical Center Institutional Review Board. Approval for the protocol was given to which data collection commenced. The primary investigator sent a request to the Data Manager of the PNA One Database -Headache such as follows: patients' demographic profile; Headache Description; Health Seeking Behavior; Diagnosis; Management; Comorbidities of Migraine; Depression Score; and Anxiety Score as tabulated in the PNA1 Database - Headache. The Data Manager then provided the data in a tabular form.

#### **Privacy**

The data will be strictly confidential and will not be accessible to the public.

#### **Outcome Measures**

**Primary outcome:** The association between Anxiety and Depression to Polypharmacy inpatients with Migraine Headache.

**Secondary outcome:** The association between the demographic profile of migraine

Table 1. Dataset in terms of area and specific indicators

DATASET	AREA	SPECIFIC INDICATOR
	Age	[years old]
	Sex	Female Male
Demographic	Educational Status	Elementary graduate Highschool graduate College graduate Postgraduate Others
	Age of onset headache	[year old]
	Frequency of headache	Per day Per week Per month
Headache Characteristics	Duration of the headache	Seconds Minutes Hours Days Daily
	Severity of the headache	No pain Little bit pain Little more pain Even more pain Much more pain Worst pain
Management of Headache	Effectiveness of the medications	Effective Initially effective but later not that effective Definitely not effective Effective but with side effects
Anxiety	Normal Borderline	0-7 8-10
	Abnormal	11-21
Depression	Normal Borderline Abnormal	0-7 8-10 11-21

PhilJNeurol 40 ISSN 0117-3391

Table 2. Sociodemographic and clinical data of the patients with Migraine

	Frequency (%); Mean ± Standard Deviation
Age (years)	38.2 ± 11.8
Sex	
Female	183 (75.3)
Male	60 (24.7)
Maic	(=)
Educational status	
Elementary graduate	121 (49.8)
High school graduate	3 (1.2)
College graduate	40 (16.5)
Postgraduate	56 (23.0)
Others	18 (7.4)
No answer	5 (2.1)
Age of onset of headache	
(years), mean + SD	24.6 (12.5)
()	()
Frequency of headache	
• •	1.00
per day	1.26
per week	1.97
per month	3.96
Duration of the headache	
Seconds	7
Minutes	0
Hours	170
Days	27
Daily	6
Coverity of the headache	
Severity of the headache	
No pain	0
Little bit pain	2
Little more pain	16
Even more pain	54
Much more pain	151
Worst pain	18
Effectiveness of the anadications	
Effectiveness of the medications	
Effective	58
Initially effective but later not that	167
effective	11
Definitely not effective	1
Effective but with side effects	·

PhilJNeurol 41 ISSN 0117-3391

patients (age, sex, educational status); headache characteristics (age of onset of headache, frequency of the headache, duration of the headache, severity of the headache); management of headache (effectiveness of the medications); Anxiety and Depression Scores to Polypharmacy.

#### **Statistical Analysis**

**Univariate analysis:** To summarize the general and clinical characteristics of the participants, descriptive statistics were employed. Nominal variables were evaluated using frequency and proportion, nonnormally distributed interval/ratio variables were assessed using median and range, and normally distributed interval/ratio variables were evaluated using mean and standard deviation. (*This is seen in table 1*).

Multivariate analysis: One-way ANOVA was used to compare the mean of the demographic and clinical profiles between the anxiety and depression score categories. The chi-square test was used to compare the frequencies between the anxiety and depression score categories. Fisher's exact test was used when frequencies were less than or equal to five (5). Significant Chisquare or Fisher's exact tests were explored further with Chi-square residuals, where values greater than two (2) or less than negative two (-2) indicate significantly different frequencies than random chance expectation. Positive values indicate significantly greater and negative values indicate less.

## Demographics of the participants RESULTS

The study participants encompasses data from 243 individuals with an average age of 38.2 years (±11.8 years). The majority of participants are female (75.3%), with males constituting 24.7% of the sample. Educational attainment varies significantly, with nearly half being elementary graduates (49.8%), while fewer have completed high school (1.2%), college (16.5%), or

postgraduate education (23.0%). The mean age of headache onset is 24.6 years (±12.5 years). Participants report headaches occurring an average of 1.26 times per day, 1.97 times per week, and 3.96 times per month. Headaches predominantly last for hours (170 cases), with some lasting for days (27 cases) and a few cases persisting daily (6 cases). Severity of headaches ranges from no pain to the worst pain, with the majority experiencing "much more pain" (151 cases). Medication effectiveness varies: 58 participants find their medications effective, 167 report initial effectiveness that diminishes over time, 11 find them definitely ineffective, and 1 experiences effectiveness with side effects.

# Sociodemographic and Clinical Variables in patients with Migraine in terms of Anxiety Score

Table 3 presents t h e sociodemographic and clinical characteristics of patients with Migraine, stratified by anxiety scores (normal: 0-7, borderline: 8-10, abnormal: 11-21). There were no significant differences among the anxiety groups in terms of age (Normal:  $38.0 \pm 12.0$ years; Borderline:  $38.0 \pm 9.8$  years; Abnormal:  $38.8 \pm 13.2$  years; p = 0.932), sex distribution (females comprising approximately 74-78% in each group; p = 0.868), educational status (p = 0.144), age of headache onset (p = 0.284), headache frequency per day, week, or month, duration of headache episodes (p = 0.444), and perceptions of medication effectiveness (p = 0.444). These findings indicate that these sociodemographic and clinical variables were comparable across different anxiety levels. However, a significant difference was observed in the severity of headaches across the anxiety categories (p = 0.026). Patients with abnormal anxiety scores were more likely to report experiencing the "worst pain" compared to those with normal or borderline scores. This suggests that higher anxiety levels may be associated with increased headache severity in patients with Migraine.

Table 3. Sociodemographic and clinical data of the patients with Migraine stratified by Anxiety Score

	Normal (0-7) n = 168	Borderline (8 – 10) n = 34	Abnormal (11-21) n = 37	p-value
	Frequency (	%); Mean ± Standa	rd Deviation	
Age (years)	38.0 ± 12.0	38.0 ± 9.8	38.8 ± 13.2	.932ª
Sex				.868c
Female Male	125 (74.4) 43 (25.6)	26 (76.5) 8 (23.5)	29 (78.4) 8 (21.6)	
Educational status				.144 <sup>f</sup>
Elementary graduate High school graduate College graduate Postgraduate Others No answer	81 (48.2) 3 (1.8) 29 (17.3) 37 (22.0) 16 (9.5) 2 (1.2)	17 (50.0) 0 (0.0) 8 (23.5) 8 (23.5) 1 (2.9) 0 (0.0)	22 (59.5) 0 (0.0) 2 (5.4) 9 (24.3) 1 (2.7) 3 (8.1)	
Age of onset of headache (years), mean + SD	24.1 ± 11.0	24.4 ± 16.1	27.7 ± 14.6	.284ª
Frequency of headache				
per day	1.18	1.64	1.35	
per week	1.79	2.61	2.41	
per month	3.42	5.36	5.59	
Duration of the headache				.444 <sup>f</sup>
Seconds	3	1	2	
Minutes	0	0	0	
Hours Days	117 18	22 2	28 7	
Daily	3	1	2	
Severity of the headache				.026 <sup>f</sup>
No pain	0	0	0	
Little bit pain	1	1	0	
Little more pain	10	4	2	
Even more pain Much more pain	39 110	9 17	5 21	
Worst pain	8	2	8	
Effectiveness of the medications				.444 <sup>f</sup>
Effective	44	1	3	
Initially effective but later not that effective	115	7	2	
Definitely not effective	6	0	0	

Statistical tests used. a: One-way ANOVA; c: Chi-square test; f: Fisher's exact test

PhilJNeurol 43 ISSN 0117-3391

## Sociodemographic and Clinical Variables in patients with Migraine in terms of Depression Score

Table 4 summarizes the sociodemographic and clinical characteristics of patients with Migraine, stratified by depression scores into normal (0-7), borderline (8-10), and abnormal (11-21) groups. There were no significant differences among these groups in terms of age (Normal:  $38.0 \pm 12.0$  years; Borderline:  $38.4 \pm 12.4$ years; Abnormal: 39.0  $\pm$  10.6 years; p = 0.991) or sex distribution (females comprising approximately 67-83% in each group; p = 0.429). Educational status was also similar across the groups (p = 0.211), with most patients being elementary graduates. The age of onset of headaches and the frequency per day, week, or month did not differ significantly, indicating that depression levels were not associated with these clinical variables.

No significant differences were observed in the duration of headache episodes among the depression groups (p = 0.482); most patients experienced headaches lasting hours. The severity of headaches was comparable across all groups (p = 0.079), with similar distributions of patients reporting various pain levels. Perceptions of medication effectiveness were consistent among the groups as well (p = 0.278), suggesting that depression levels did not influence patients' views on the efficacy of their migraine treatments.

We have insufficient evidence to demonstrate whether depression scores has a significant association with the sociodemographic or clinical variables studied in patients with Migraine. Unlike anxiety levels, which showed a significant relationship with headache severity, depression did not appear to influence the clinical presentation or perceived treatment effectiveness in this patient population. Clinicians should consider that while depression is important for overall patient care, it may not directly affect migraine characteristics as measured in this study.

#### Polypharmacy and Medication related to Anxiety Score

The data on anxiety scores and polypharmacy reveals interesting correlations between medication use and anxiety levels. Among the 74 participants, those classified with normal anxiety (scores o-7) have a mean polypharmacy score of 1 drug (±13), with 20 individuals taking more than one drug and 5 not using any medications. In contrast, participants with borderline anxiety scores (8-10) have a slightly higher mean polypharmacy score of 8 drugs (±8), with 8 taking more than one drug and 2 reporting no medication use. Those with abnormal anxiety scores (11-21) show a mean polypharmacy score of 5 drugs (±5), with 9 individuals using more than one drug and 4 not on any medication. This distribution suggests a trend where higher anxiety levels are associated with increased use of multiple medications, although the data also indicates a notable number of participants in each anxiety category not using medications.

To further investigate the significant association between anxiety levels and headache severity observed in Table 2, we performed a chi-square residual analysis (Table 6). Chi-square residuals quantify the difference between the observed and expected frequencies in each category, highlighting which specific groups contribute most to the overall association. In our analysis, patients with abnormal anxiety scores had a residual of 3.185 for reporting "worst pain," exceeding the critical value of 1.96, indicating a statistically significant higher number of patients in this group reported the worst pain than expected by chance. Conversely, the normal anxiety group had a residual of -1.332 for the "worst pain" category, suggesting fewer patients reported the worst pain than expected, though this did not reach statistical significance. Residuals for other pain severity levels did not exceed the critical value, indicating no significant deviations from expected frequencies in those categories. These findings enhance the interpretability of Table 2 by pinpointing that the significant difference in headache severity

Table 4. Sociodemographic and clinical data of the patients with Migraine Headache stratified by Depression Score

	Normal (0-7) n = 189	Borderline (8-10) n=29	Abnormal (11-21) n = 21	p-value
	Frequency	(%); Mean ± Standa	ard Deviation	
Age (years)	38 ±12.0	38.4 ± 12.4	39.0 ± 10.6	.991ª
Sex				.429°
_	142 (75.1)	24 (82.8)	14 (66.7)	
Female Male	47 (24.9)	5 (17.2)	7 (33.3)	
Educational status				.211f
Clamantam, avaduata	02 (40 2)	16 (FF O)	11 (50 4)	
Elementary graduate High school graduate	93 (49.2) 3 (1.6)	16 (55.2) 0 (0.0)	11 (52.4) 0 (0.0)	
College graduate	33 (17.5)	3 (10.3)	3 (14.3)	
Postgraduate	42 (22.2)	9 (31.0)	3 (14.3)	
Others	16 (8.5)	1 (3.4)	1 (4.8)	
No answer	2 (1.1)	0 (0.0)	3 (14.3)	
Age of onset of headache (years), mean + SD	24.2 ± 11.4	24.0 ± 17.7	29.9 ± 12.4	.945ª
requency of headache				
per day	1.19	1.14	2.14	
per week	1.9	2.24	2.57	
per month	4.01	4.34	3.71	
Duration of the headache				.482 <sup>f</sup>
Seconds	4	0	2	
Minutes	0	0	0	
Hours	130	20	17	
Days	19	4	4	
Daily	5	0	1	
Severity of the headache				.079f
No pain	0	0	0	
Little bit pain	1	0	1	
Little more pain	11	3	2	
Even more pain	43	7	3	
Much more pain	121	17	10	
Worst pain	12	1	5	
Effectiveness of the medications				.278 <sup>f</sup>
Effective	48	1	1	
Initially effective but later not that effective	46 134	4	1	
Definitely not effective	5	1	0	
Effective but with side effects	0	0	0	

Statistical tests used. a: One-way ANOVA; c: Chi-square test; f: Fisher's exact test

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across anxiety levels is primarily driven by the increased reporting of "worst pain" among patients with abnormal anxiety scores.

Table 6 presents the distribution of polypharmacy among patients with Migraine, stratified by anxiety score categories (normal, borderline, and abnormal). The Fisher's exact test yielded a p-value of 0.640, indicating no statistically significant association between anxiety scores and polypharmacy levels. This suggests that the number of medications taken by patients does not differ significantly across different anxiety levels, implying that anxiety status does not influence the extent of polypharmacy in this patient population.

#### Polypharmacy and Medication related to Depression Score

The data on depression scores and polypharmacy illustrates how medication use varies with depression severity. Among the 73 participants, those with normal depression scores (0-7) have a mean polypharmacy score of 1 drug (±15), with 26 individuals taking more than one drug and 5 not on any medication. Participants with borderline depression scores (8-10) have a mean polypharmacy score of 6 drugs (±6), with 8 using multiple medications and 2 reporting no medication use. In the group with abnormal depression scores (11-21), the mean polypharmacy score is 3 drugs (±3), with 3 individuals taking more than one drug and 3 not using any medications. This data indicates that as depression severity increases, there tends to be a higher mean number of drugs taken, though a proportion of individuals in each depression category are not using medications.

Table 7 presents the distribution of polypharmacy among patients with Migraine, stratified by depression score categories (normal, borderline, and abnormal). The Fisher's exact test yielded a p-value of 0.476, indicating no statistically significant association between depression scores and polypharmacy levels. This suggests that the

number of medications taken by patients does not differ significantly across different depression levels, implying that depression status does not influence the extent of polypharmacy in this patient population.

#### DISCUSSION

The average age of study participants have a mean age of 38.2 years (±11.8 years), indicating a middle-aged population. The majority of participants are female (75.3%), suggesting that the sample may be reflective of a population where headache disorders are more prevalent among women. Research supports that headaches, particularly migraines, are more common in women compared to men (Buse et al., 2015).

A significant portion of participants are elementary school graduates (49.8%), with a smaller fraction completing high school (1.2%) or higher education levels (college 16.5%, postgraduate 23.0%). This variation in educational attainment may influence access to healthcare and awareness of headache management strategies. Lower educational attainment has been linked to lower health literacy, which might affect the perception and management of headaches.6 The high proportion of elementary school graduates compared to those with higher education levels suggests that educational attainment may influence the management and understanding of headache disorders.

The mean age of headache onset is 24.6 years (±12.5 years), indicating that headaches generally begin in early adulthood. This aligns with patterns observed in the literature, where migraines and other headache types often start in adolescence or early adulthood.<sup>3</sup> Participants report experiencing headaches 1.26 times per day, 1.97 times per week, and 3.96 times per month. This frequency is indicative of a chronic headache pattern. Chronic headache disorders, such as chronic migraines or tension-type headaches, can significantly impact daily functioning and quality of life.<sup>2</sup>

Table 5. Contingency table post-hoc residuals

	Normal	Borderline	Abnormal
	(0-7)	(8 – 10)	(11-21)
	n = 168	n = 34	n = 37
Severity of the headache  No pain Little bit pain Little more pain Even more pain Much more pain Worst pain	- -0.351 -0.398 0.233 0.497 -1.332	1.367 1.187 0.596 -0.795 -0.320	- -0.551 -0.276 -1.075 -0.312 3.185

Table 6. Polypharmacy in Patients with Migraine stratified by Anxiety Score

	Anxiety Score				
Polypharmacy	Normal (0-7)	Borderline (8-10)	Abnormal (11-21)	Total	
0	5	2	5	12	
1	13	8	5	26	
Greater than 1	20	8	9	36	
Total	38	18	18	74	

Fisher's exact test p-value = 0.640

Table 7. Polypharmacy in Patients with Migraine stratified by Depression Score

	Depression Score			
Polypharmacy	Normal (0-7)	Borderline (8-10)	Abnormal (11-21)	Total
0 1 Greater than 1 Total	5 15 26 48	2 6 8 16	3 3 3 9	10 24 37 73

Fisher's exact test p-value = 0.476

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Headaches predominantly last for hours (170 cases), with a smaller number lasting for days (27 cases) or occurring daily (6 cases). The predominance of hours-long headaches suggests a mix of acute and chronic headache types. For chronic headaches, longer durations are often reported.<sup>10</sup>

Most participants experience "much more pain" (151 cases), reflecting a high level of discomfort. Severity is a critical factor in evaluating headache impact and management. Severe headaches often require more aggressive treatment and management strategies.8

The effectiveness of medications varies: 58 participants find medications effective, 167 report initial effectiveness that diminishes over time, 11 find them definitely ineffective, and 1 experiences effectiveness with side effects. The high number of participants experiencing diminishing effectiveness over time suggests that tolerance to medication might be an issue. This is consistent with findings that some individuals may experience reduced efficacy of headache treatments over time or due to the development of medication overuse.<sup>4</sup>

There was no association between Polypharmacy and Anxiety and Depression scores in patients with Migraine. However, patients with higher anxiety levels are more likely to report experiencing the "worst pain" compared to those with normal or borderline anxiety scores, indicating a possible link between increased anxiety and reporting of severe migraine headaches. On the other hand, there is insufficient evidence to show a significant association between depression scores and sociodemographic or clinical variables in patients with Migraine. Unlike anxiety, which was linked to headache severity, depression did not appear to influence the clinical presentation or treatment effectiveness. While depression remains important for overall patient care, it may not directly impact migraine characteristics in this population.

The number of medications taken by patients does not significantly differ across depression and anxiety levels, indicating that depression and anxiety status does not impact the extent of polypharmacy. The data suggests that the patients experience significant challenges with headache management, including high pain levels, varying medication effectiveness, and a predominant pattern of headaches lasting hours. These insights highlight the need for targeted interventions and possibly a reevaluation of treatment approaches to improve management outcomes for individuals suffering from headaches.

#### CONCLUSION

The study highlights that participants, primarily middle-aged women, experience chronic headaches with high pain severity, often lasting for hours. Educational attainment may influence headache management compliance with a large proportion having only elementary education. Headache onset typically begins in early adulthood, and medication effectiveness often diminishes over time suggesting potential tolerance issues. Anxiety is associated with reporting of increased headache severity while depression does not significantly impact headache characteristics or polypharmacy. The findings emphasize the need for targeted interventions and revised treatment strategies to improve headache management outcomes.

#### **REFERENCES**

- 1. Baraldi, F. A. (2016). Polypharmacy Among Headache Patients: A Cross-Sectional Study. *CNS Drugs*, 6(36), 567-578. <a href="https://doi.org/10.1007/s40263-018-0522-8">https://doi.org/10.1007/s40263-018-0522-8</a>
- 2. Bigal, M. E., & Lipton, R. B. (2008). The epidemiology, burden, and comorbidities of migraine. Neurology, *37*(4), 631–649.

- 3. Breslau, N., Lipton, R. B., Stewart, W. F., Schultz, L. R., & Welch, K. M. (2003). Comorbidity of migraine and depression: investigating potential etiology and prognosis. Neurology, 60(9), 1308-1312.
- 4. Diener, H. C., Holle, D., Solbach, K., & Gaul, C. (2016). Medication-overuse headache: risk factors, pathophysiology and management. *Nature reviews*. *Neurology*, *12*(10), 575–583. https://doi.org/10.1038/nrneurol.2016.124.
- Halli-Tierney, A. D. (2019).
   Polypharmacy: Evaluating Risks and Deprescribing. American Family Physician, 1(100), 32-38. American Family Physician. 31259501
- 6. Hibbard J. H. (2003). Engaging health care consumers to improve the quality of care. Medical care, 41(1 Suppl), I61–I 7 0. https://doi.org/10.1097/00005650-200301001-00007
- Kasteridis, P. (2019). Association between antipsychotic polypharmacy and outcomes for people with serious mental illness in England. *Psychiatry Services*, 70(8), 650-656. American Psychiatry Association. 10.1176/ appi.ps.201800504
- 8. Lipton, R. B., Diamond, S., Reed, M., Diamond, M. L., & Stewart, W. F. (2001). Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache*, 41(7), 638–645. <a href="https://doi.org/10.1046/j.1526-4610.2001.041007638.x">https://doi.org/10.1046/j.1526-4610.2001.041007638.x</a>
- 9. Masnoon, N. (2017). What is polypharmacy? A systematic review of definitions. *BMC Geriatrics*, 17(1), 230. PubMed. 10.1186/s12877-017-0621-2
- 10. Murphy C, Hameed S. Chronic Headaches. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <a href="https://">https://</a>

- www.ncbi.nlm.nih.gov/books/ NBK559083/
- 11. Muth, C. (2018). Evidence supporting the best clinical management of patients with multimorbidity and polypharmacy: a systematic guideline review and expert consensus. *Journal of Internal Medicine*, *285*(3), 272-288. Wiley. 10.1111/joim.12842
- 12. Palapinyo, S. (2021). Association between polypharmacy and depression: a systematic review and meta-analysis. *J Pharm Pract Res*, *51*, 260-299. https://doi.org/10.1002/jppr.1749
- 13. Putnam G, O'Quinn S, Bolden-Watson C, Davis R, Gutterman D, Fox A. Migraine Polypharmacy and the Tolerability of Sumatriptan: A Large-Scale, Prospective Study. Cephalalgia. 1999;19(7):668-675. doi:10.1046/j.1468-2982.1999.019007668.x
- 14. Snaith, R. (1990, August). The Hospital Anxiety and Depression (HADS) scale. *The Hospital Anxiety and Depression (HADS) scale*, 40(1), 305. PubMed. 10.1192/pb.16.7.451
- 15. Tseng, H.-M. (2019). Developing a measure of medication-related quality of life for people with polypharmacy. *Quality of Life Research*, *25*(5), 1295-1302. SprinerLink. 10.1007/s11136-015-1177-2
- 16. Van Wilder, L. (2022). Polypharmacy and Health-Related Quality of Life/ Psychological Distress Among Patients With Chronic Disease. *Preventing Chronic Disease*, 19(E50). National Library of Medicine. 10.5888/ pcd19.220062
- 17. Wood ME, Burch RC, Hernandez-Diaz S. Polypharmacy and comorbidities during pregnancy in a cohort of women with migraine. Cephalalgia. 2 0 2 1; 4 1 (3): 3 9 2 4 0 3. doi:10.1177/0333102420975394

PhilJNeurol 49 ISSN 0117-3391

18. Zahlan, G. (2023). Polypharmacy and Excessive Polypharmacy Among Persons Living with Chronic Pain: A Cross-Sectional Study on the Prevalence and Associated Factors. *Journal of Pain Research*, 16(1), 3085-3100. Dovepress. 10.2147/ JPR.S411451

PhilJNeurol 50 ISSN 0117-3391

#### Appendix. Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate is best.

D	Α		D	Α	
		I feel tense or wound up			I feel as if I am slowed down
	3	Most of the time	3		Not at all
	2	A lot of the time	2		Sometimes
	1	From time to time, occasionally	1		Very often
	0	Not at all	0		Nearly all the time
		I still enjoy things I used to enjoy			I get a sort of frightened feeling like "butterflies" in my stomach
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite often
3		Hardly at all		3	Very Often
		I get sort of a frightened feeling as if something awful is about to happen			I have lost interest in my appearance
	3	Very definitely and quite badly	3		I take just as much care as ever
	2	Yes, but not too badly	2		I may not take quite as much care
	1	A little bit but it doesn't really worry me	1		I don't take as much care as I should
	0	Not at all	0		Definitely
		I can laugh and see the funny side of things			I feel restless as I have to be on the move
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind			I look forward with enjoyment to things
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful			I get sudden feelings of panic
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Very seldom
		I can sit at ease and feel relaxed			I can enjoy a good book or radio or TV program
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not often	2		Not often
	3	Not at all	3		Very seldom
Dloor		and that you have answered all the guestions	-		

Please check that you have answered all the questions.

Scoring:
Total Score: Depression (D): \_\_\_\_\_ Anxiety (A): \_\_\_\_\_

0-7: Normal 8-10: Borderline abnormal (borderline case) 11-21: Abnormal (case)

PhilJNeurol 51 ISSN 0117-3391