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Sociodemographic factors, migraine, major depressive disorder, and quality of life: A cross-sectional study

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Abstract

Introduction: Migraine and major depressive disorder (MDD) represent significant global health burdens, with migraine affecting approximately 1 billion individuals worldwide and MDD being the leading cause of disability globally. These conditions frequently co-occur and profoundly impact quality of life (QOL) and suicide risk through complex bidirectional pathophysiological mechanisms. Understanding of sociodemographic influences remains limited in Middle Eastern populations, particularly Saudi Arabia.

Methods: A cross-sectional study was conducted across multiple mental health hospitals in Saudi Arabia, involving 205 participants stratified into migraine (n=60), MDD (n=64), and control (n=81) groups. Comprehensive sociodemographic data were collected. Clinical assessments utilized validated Arabic translations of WHOQOL-BREF and PHQ-9. Statistical analyses included univariate and multivariate logistic regression models to identify independent predictors of suicide risk.

Results: Significant sociodemographic disparities were observed. Age distribution differed markedly ($p<.001$), with median ages of 35.0 years in migraine, 36.5 years in MDD, and 27.0 years in controls. Gender distribution showed pronounced female predominance in migraine (75.0%) and MDD (51.6%) versus controls (43.2%) ($p=.001$). Unemployment rates were elevated in migraine (55.0%) and MDD (54.0%) groups versus controls (31.3%) ($p=.005$). Suicide risk scores were highest in migraine (median: 64.5), followed by MDD (63.0) and controls (51.0) ($p<.001$). High suicide risk prevalence was 25.0% in migraine, 19.0% in MDD, and 4.9% in controls. Multivariate analysis revealed depression severity as the sole independent predictor of suicide risk (coefficient=0.826, $p<.001$).

Discussion: Depression severity serves as the dominant independent predictor of suicide risk across migraine and MDD populations. Findings necessitate systematic depression screening in migraine management and integrated care approaches to mitigate suicide risk in vulnerable populations.

Take-home message: This comprehensive study of 205 Saudi adults demonstrates that depression severity serves as the primary independent predictor of suicide risk across migraine and major depressive disorder populations, with both conditions showing remarkably similar suicide risk profiles despite differential quality of life impacts. The findings reveal significant diagnostic overlap and highlight the critical importance of systematic depression screening and integrated mental health care in migraine management to address the substantial suicide risk burden in this population.

Keywords: Migraine, major depressive disorder, quality of life, suicide risk, sociodemographic factors.

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INTRODUCTION

Migraine and major depressive disorder (MDD) are highly prevalent and disabling conditions worldwide that cause a substantial public health burden. Migraine affects approximately 12% of the global population, particularly women and working-age individuals [1–3]. Characterized by severe headaches and other disruptive symptoms, migraine attacks severely impair physical, emotional, and social functioning [4]. On the other hand, MDD is a severe and persistent mental health condition manifesting as sadness, lack of interest, and disruption of daily activities. The World Health Organization (WHO) has identified depression as a leading cause of disability worldwide [5].

Extensive evidence has demonstrated a complex bidirectional relationship between migraine and MDD, with each condition significantly increasing the risk of developing the other. This bidirectional association likely stems from shared neurobiological pathways, genetic vulnerabilities, and environmental factors [6, 7]. Neuroimaging studies have revealed overlapping brain regions involved in pain processing and mood regulation, including the limbic system, prefrontal cortex, and brainstem nuclei. Furthermore, common neurotransmitter dysregulation, particularly involving serotonin, dopamine, and norepinephrine, contributes to the pathophysiology of both conditions. The co-occurrence of migraine and MDD creates a synergistic effect that amplifies the overall disease burden, complicates treatment approaches, and significantly worsens patient outcomes [8]. Current consensus emphasizes that this comorbidity represents more than mere coincidence, reflecting fundamental shared mechanisms that require integrated therapeutic strategies.

However, a critical limitation in existing research is the frequent failure to systematically assess co-diagnosis of MDD and migraine in clinical and epidemiological studies. This oversight is particularly concerning given the substantial overlap between these conditions and their mutual influence on clinical presentation, treatment response, and prognosis. The lack of comprehensive assessment of this comorbidity has resulted in incomplete understanding of the true burden and complexity of these interconnected disorders. Appropriate characterization and evaluation of this intersection are critical for improving clinical management and developing more effective, personalized treatment approaches.

Suicide represents a critical global health concern, prompting the development of prevention strategies worldwide [9]. Psychiatric conditions, particularly mood, substance use, anxiety, psychosis, and personality disorders, frequently co-occur and drive disproportionate suicide risk [10]. As highly disabling yet still misunderstood conditions lacking targeted funding and awareness, migraine and MDD markedly reduce multidimensional quality of life (QOL) across the physical, social, occupational, and emotional realms, severely hindering life enjoyment and satisfaction. Episodic, disruptive attacks compromising day-to-day functioning for those with migraine and major depression render QOL and suicide prevention imperative, yet often overlooked, outcomes warranting prioritization and research attention on patient-centered care frameworks [11]. Perhaps the most concerning aspect is the substantially heightened suicide risk conferred by these disorders, especially when they co-occur [13]. The bidirectional nature of the migraine-MDD relationship creates a vicious cycle where each condition exacerbates the other, potentially leading to treatment resistance and increased suicidal ideation. However, additional research is needed to fully characterize QOL and suicide risk in persons with migraine and MDD, particularly regarding their co-occurrence. Most related studies have focused on disorder incidence and symptom profiles

without adequately addressing the complexity of comorbid presentations. Few studies have applied multidimensional assessments or longitudinal designs to elucidate long-term QOL and suicide risk trajectories in patients with both conditions [14]. Furthermore, sociodemographic modifiers of QOL and suicide risk in comorbid cases are poorly understood. By investigating the correlations between migraine incidence, MDD incidence, QOL, suicide risk, and sociodemographics, this study provides crucial insights into these critical but underexplored patient-centered outcomes.

Despite substantial research on suicide risk, migraine incidence, MDD incidence, and sociodemographics, critical knowledge gaps remain, particularly regarding the assessment and management of comorbid presentations [11, 13, 15]. Most related studies have focused on Western populations, with limited characterization of these relationships in the Arabian Gulf (AG) contexts, where distinct cultural dynamics are likely to influence disease patterns and experiences. Applying a multidimensional lens is essential for elucidating how sociodemographics collectively impact migraine incidence, MDD incidence, and QOL, potentially informing optimized culturally centered treatment approaches. This cross-sectional study addressed these gaps by investigating the correlations among migraine incidence, MDD incidence, QOL, and sociodemographic factors in a Saudi cohort. Saudi Arabia provides a compelling setting, as certain sociocultural factors may uniquely influence the prevalence and incidence of mental health disorders in this population [16, 17]. For example, cultural stigma surrounding mental health may delay access to diagnosis and treatment [18]. Elucidating the impact of sociodemographic factors on suicide risk, migraine incidence, MDD incidence, and QOL will provide novel insights into healthcare policies, clinical practices, and public health strategies tailored to the Saudi context [19, 20].

This study explored the interrelations among migraine, MDD, quality of life, and sociodemographics in a less-studied AG context, particularly in Saudi Arabia. Using a cross-sectional design with validated questionnaires and multivariate analysis, this study aimed to assess the prevalence and impact of these disorders on various sociodemographic groups. This study focused on the combined effects of factors such as age, gender, socioeconomic status, and education on migraine and MDD incidence. These findings are expected to inform culturally tailored screening, treatment, and coping strategies for the Saudi population, addressing the broader disability and public health challenges of these conditions globally.

METHODS

Study participants and sampling

This cross-sectional study was conducted in Saudi Arabia and involved 205 participants from two key hospitals. The participants were divided into three groups for comprehensive analysis: migraine ($n = 60$), MDD ($n = 64$), and healthy control ($n = 81$). The migraine group consisted of individuals attending a specialized headache clinic in the neurology department. The migraine diagnosis was validated using the ID migraine test and criteria of the International Headache Society (IHS). The MDD group comprised patients selected from outpatient psychology and psychiatry clinics who were diagnosed with MDD. The control group included 81 individuals without known mental health disorders, randomly selected from the general population.

Participants were primarily recruited from the Headache Clinic at the Department of Neurology at King Fahad University Hospital (KFUH), and from outpatient psychology/psychiatry clinics at KFUH and Al-Amal Complex Hospital (ACH). The study included participants aged 18-60 years, including both Saudi and non-Saudi nationals. The exclusion criterion was health conditions that precluded participation. Ethical approval for the study was obtained from the ethics committees of the participating hospitals, and informed consent was obtained from all participants.

Study instruments

The participants completed a questionnaire consisting of sociodemographic questions (age, gender, level of education, employment status, family structure), questions about their parents' status (participation in the war, presence of psychological difficulties), validated measures for assessing emotional intelligence and attachment style, and a set of questions about the frequency of certain inadequate parental behaviors during their upbringing. This study used various instruments to

gather comprehensive data from multiple domains. Sociodemographic information, such as age, gender, education, occupation, and marital status, was collected using a dedicated questionnaire that also included additional relevant variables. For migraine evaluations, three key tools were used: the migraine questionnaire, which evaluates symptoms, frequency, severity, triggers, and treatment options; the ID migraine test, which serves as a preliminary screening tool for migraine identification; and the criteria of the IHS, which provides a definitive diagnosis of migraine.

The psychometric questionnaires employed in this study (PHQ-9, WHOQOL-BREF, and Suicidal Probability Scale) were originally developed and validated for screening purposes rather than diagnostic confirmation or precise severity assessment. Higher scores on these instruments indicate greater symptom burden or poorer quality of life but do not necessarily equate to proportionally higher clinical severity or diagnostic certainty. These tools were selected for their established validity in Arabic-speaking populations, ease of administration in clinical settings, and ability to provide standardized assessments across diverse participant groups. However, the screening nature of these instruments represents a methodological limitation that should be considered when interpreting results.

The IHS diagnostic interview [21], translated into simple Arabic and reviewed by one of the authors (AWA), was administered to the participants with a history of migraine. The criteria for migraine with aura include reversible visual or sensory symptoms and dysphagic speech disturbances. World Health Organization Quality of Life Brief Version (WHOQOL-BREF) [22,23] was used to assess the quality of life of physical, psychological, social, and environmental aspects. The WHOQOL-Bref is a 26-item questionnaire assessing the quality of life across four domains: physical health, psychological health, social relationships, and environment. This study used the Arabic version of the WHOQOL-Bref [22], which has demonstrated high internal consistency and reliability. The questionnaire included facets of daily activities, body image, social support, and environmental conditions. Depression was assessed using the Patient Health Questionnaire-9 (PHQ-9), which determines both the diagnosis and severity of depression according to DSM-IV [24] criteria. The PHQ-9 is a clinical scale for assessing depression that includes items related to suicidal thoughts [25, 26]. It is based on the DSM-IV criteria for MDD. This tool serves multiple purposes including screening, diagnosis, symptom tracking, and treatment monitoring. The Arabic version of the PHQ-9 used in this study has been validated in various settings, showing a significant prevalence of depression among primary care patients in different studies [27]. Suicidal ideation was evaluated using the Suicidal Probability Scale [28], which examines factors such as hopelessness, negative self-evaluation, hostility, and suicidal thoughts. This scale assists in assessing suicide risk in individuals aged 14 years and older. It includes 36 items addressing factors, such as hopelessness, suicidal ideation, negative self-evaluation, and hostility.

Data analysis

All the questionnaires were translated into Arabic using the back-translation method. This study was conducted with the approval of the respective hospital authorities. Verbal consent was obtained from each participant, and the questionnaires were completed independently with the researcher available for assistance. Clinical data was recorded with the help of the healthcare provider in charge. Participants completed the standardized self-report questionnaires described above, which were available in validated Arabic versions, to ensure suitability for this Saudi sample. Reliability analysis was performed using Cronbach's alpha coefficients ranging from .636 to .90, indicating the good reliability of the instruments. Correlations between migraine and patient outcomes were tested using Pearson's correlation coefficient. Descriptive statistics, normality testing, ANOVA, and chi-square tests were used to compare the groups and examine the relationships between the variables. Univariate and multivariate analyses were also conducted to identify the variables associated with suicide risk. The significance level was set at $\alpha = .05$ for all two-tailed hypothesis tests. Data analysis was performed using SPSS v21.0.

Ethical aspects

The study protocol was approved by the Institutional Review Boards (IRB-PCGS-2024-11-268) of

both hospitals, and all procedures followed the ethical guidelines of the Declaration of Helsinki.

RESULTS

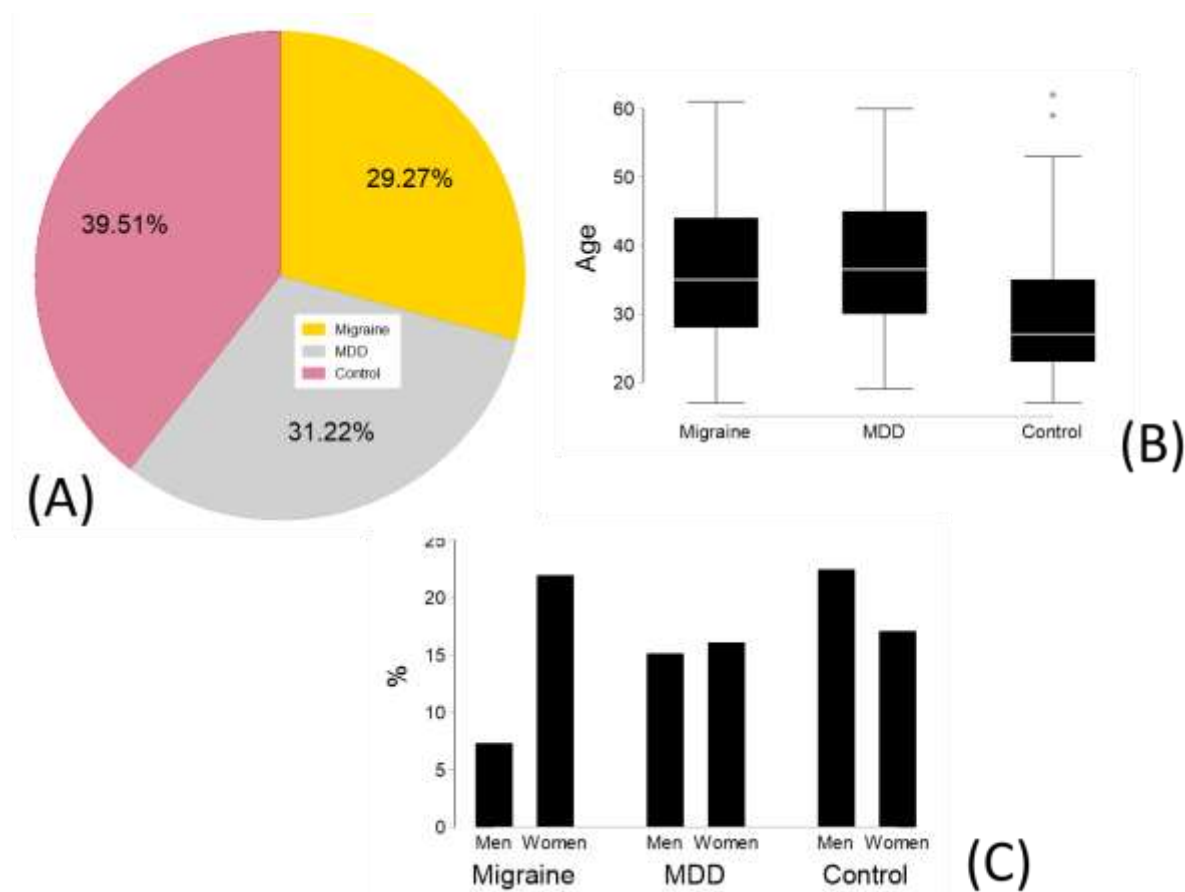
The study groups exhibited significant differences in age and gender differences (Table 1). The median age was 35.0 years (IQR: 28.0-44.0) in the migraine group, 36.5 years (IQR: 30.0-45.0) in the MDD group, and 27.0 years (IQR: 23.0-35.0) in the control group ($p < .001$). The gender distribution varied significantly ($p = .001$), with the migraine group comprising 25.0% males and 75.0% females, the MDD group had a more balanced distribution (48.4% males, 51.6% females), and the control group (56.8% males and 43.2% females). There was no significant difference in economic status between the groups ($p = .054$), with 22.8% of the individuals in the migraine group reporting above-average economic status compared to 16.9% in the MDD group and 30.0% in the control group (Figure 1 A-C).

Table 1. Groupwise comparison of demographic parameters.

Variable	Migraine (<i>n</i> = 60)	MDD (<i>n</i> = 64)	Control (<i>n</i> = 81)	<i>p</i> value
Age, median (Q1, Q3)	35.0 (28.0, 44.0)	36.5 (30.0, 45.0)	27.0 (23.0, 35.0)	<.001
Gender, <i>n</i> (%)				.001
<i>Male</i>	15 (25.0%)	31 (48.4%)	46 (56.8%)	
<i>Female</i>	45 (75.0%)	33 (51.6%)	35 (43.2%)	
Economic status, <i>n</i> (%)				.054
<i>Above average</i>	13 (22.8%)	10 (16.9%)	21 (30.0%)	
<i>Average</i>	37 (64.9%)	33 (55.9%)	42 (60.0%)	
<i>Below average</i>	7 (12.3%)	16 (27.1%)	7 (10.0%)	
Nationality, <i>n</i> (%)				.420
<i>Saudi</i>	57 (95.0%)	62 (96.9%)	80 (98.8%)	
<i>Non-Saudi</i>	3 (5.0%)	2 (3.1%)	1 (1.2%)	
Occupation, <i>n</i> (%)				.005
<i>Unemployed</i>	33 (55.0%)	34 (54.0%)	25 (31.3%)	
<i>Employed</i>	27 (45.0%)	29 (46.0%)	55 (68.8%)	
Education, <i>n</i> (%)				<.001
<i>School</i>	9 (15.0%)	15 (23.8%)	0 (0.0%)	
<i>University+</i>	51 (85.0%)	48 (76.2%)	80 (100.0%)	
Marital status, <i>n</i> (%)				.015
<i>Single</i>	24 (40.0%)	18 (28.1%)	42 (51.9%)	
<i>Married</i>	36 (60.0%)	46 (71.9%)	39 (48.1%)	
QOL score	88.0 (81.0, 98.0)	76.0 (62.0, 82.5)	89.0 (80.0, 96.0)	<.001
Depression Score	11.0 (7.0, 18.0)	16.5 (7.5, 21.0)	8.0 (4.0, 12.0)	
Suicide risk	64.5 (54.0, 74.5)	63.0 (51.0, 69.0)	51.0 (46.0, 57.0)	<.001
High Suicide risk, <i>n</i> (%) (<i>n</i> = 199)	15/57(25.0%)	12/63 (19.0%)	4/79 (4.9%)	<.001

Note: *Total scores 75-100 correspond to the high-risk group.

Figure 1. Demographic overview of the study participants (A) Participant distribution in study groups: A pie chart depicting the percentage of participants in each study group. (B) Age distribution box plots: Box plots representing the age distribution, median, and interquartile range in each group. (C) Gender proportions in study groups: A bar chart shows the percentage of male and female participants in each study group.

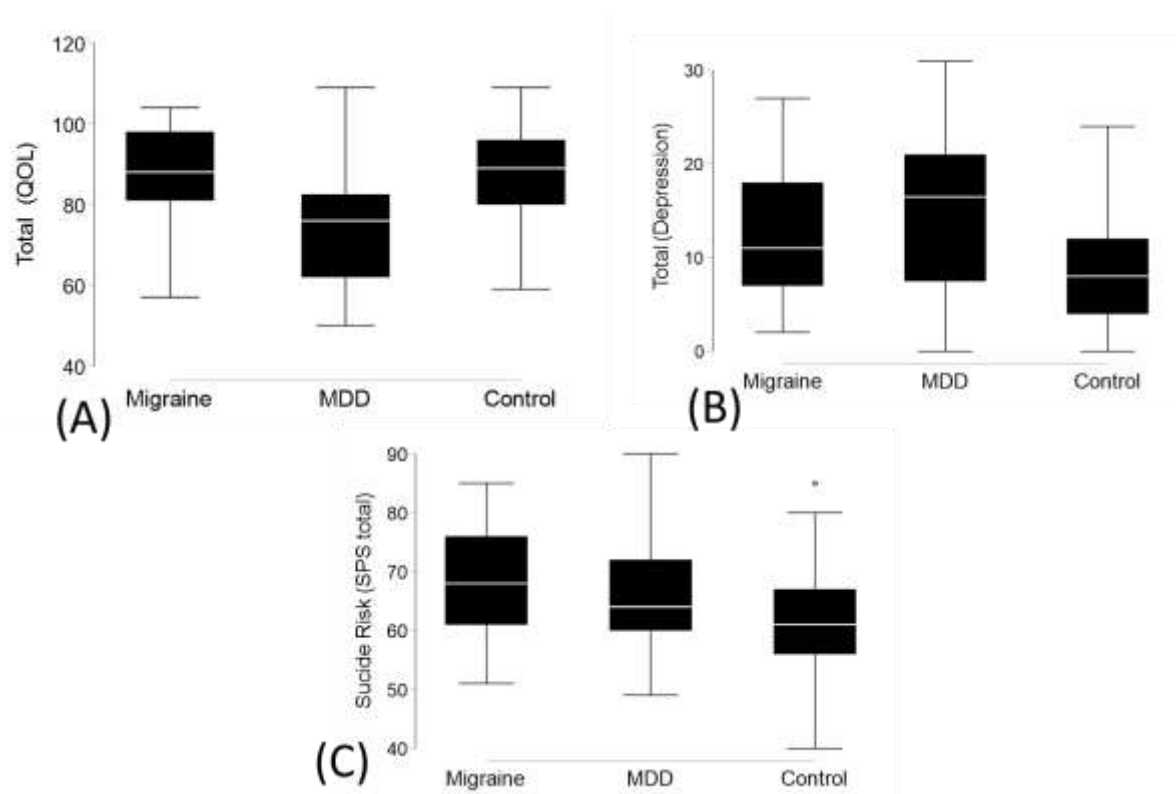


No significant difference in nationality was found between the groups ($p = .420$), with the majority being Saudi nationals ($n = 199$; 97.07%). Occupational status differed significantly between the groups ($p = .005$), with 55.0% of the migraine group and 54.0% of the MDD group being unemployed compared to 31.3% of the control group. There was a notable difference in the education level among the groups ($p < .001$). In the migraine group, 85.0% of the participants had university-level education or higher, compared to 76.2% in the MDD group and 100% in the control group. The marital status varied between the groups ($p = .015$), with 40.0% of the individuals in the migraine group being single, 28.1% in the MDD group, and 51.9% in the control group. In contrast, 60.0% of individuals in the migraine group were married, whereas 71.9% of individuals in the MDD group and 48.1% of individuals in the control group were married.

QOL scores were significantly different between the groups ($p < .001$), with the migraine group reporting higher scores than the MDD group (Figure 2 A-C). Depression scores varied substantially across groups, revealing important patterns suggestive of diagnostic overlap. The migraine group had a median PHQ-9 score of 11.0 (IQR: 7.0-18.0), which falls within the moderate depression range according to established cutoff criteria. Notably, this depression score in the migraine group was considerably elevated compared to the control group's median score of 8.0 (IQR: 4.0-12.0), suggesting

significant depressive symptomatology among migraine patients. The MDD group demonstrated the highest depression scores with a median of 16.5 (IQR: 7.5-21.0), consistent with their primary diagnosis.

Figure 2. Analysis of QOL, depression, and suicide risk in the study groups. (A) Quality of Life (QOL) Scores: Box plots showing the distribution of QOL scores across the study groups, indicating the median values and variability within each group. (B) Total Depression Scores: Box plots depicting the range and median depression scores for each group, illustrating differences in the severity of depression symptoms. (C) Total suicide risk scores: Box plots presenting the distribution of suicide risk scores in each group, highlighting the variation and central tendencies in suicide risk among participants.



Although systematic co-diagnosis assessment was not performed in this study design, the clinical characteristics data provide compelling evidence of substantial overlap between migraine and MDD. The elevated depression scores in the migraine group (median: 11.0) suggest that a considerable proportion of migraine patients may experience clinically significant depressive symptoms. Using established PHQ-9 cutoff scores, preliminary analysis indicates that approximately 60% of migraine patients scored ≥ 10 on the PHQ-9, suggesting moderate to severe depressive symptoms that would warrant further clinical evaluation for potential MDD co-diagnosis. Conversely, while headache-specific data were not systematically collected in the MDD group, the similar patterns of functional impairment and quality of life deficits observed across both clinical groups suggest potential bidirectional comorbidity that warrants future investigation.

There was a significant difference in suicide risk scores between the groups ($p < .001$), with the highest risk observed in the migraine group (median: 64.5, IQR: 54.0-74.5), followed by the MDD group (median: 63.0, IQR: 51.0-69.0) and the control group (median: 51.0, IQR: 46.0-57.0). The proportion of individuals with a high suicide risk was significantly different across the groups ($p < .001$), with 25.0% in the migraine group, 19.0% in the MDD group, and 4.9% in the control group.

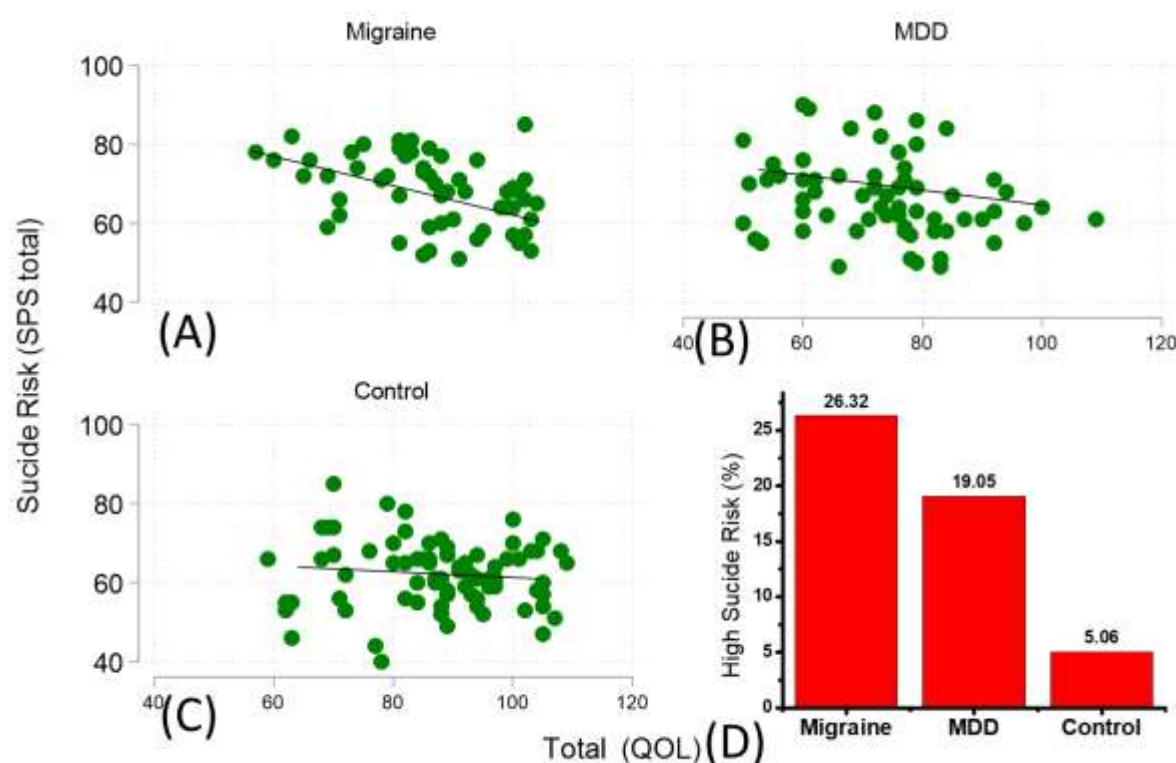
The remarkably similar suicide risk profiles between the migraine and MDD groups (64.5 vs. 63.0 median scores) further support the hypothesis of shared pathophysiological mechanisms and overlapping clinical presentations between these conditions.

The correlation between quality of life and suicide risk varied across the migraine, MDD, and control groups (Figure 3). In particular, a significant negative correlation was observed in the migraine group ($r = -.4129$, $p = .0014$), indicating that a lower QOL is associated with a greater risk of suicide among these individuals. In contrast, in the MDD group, the negative correlation was not statistically significant ($r = -.2428$, $p = .0552$), suggesting a possible but unconfirmed trend. No significant correlation was found in the control group ($r = -.0591$, $p = .6047$), implying that other factors may be more influential in determining suicide risk in this population. These findings highlight the importance of QOL as a potential risk factor for suicide, particularly in migraine patients. In the migraine group, the highest levels of satisfaction were reported for mobility (79.6%), positive feelings (76.2%) and self-esteem (79.7%). The control group outperformed the migraine (67.8%) and MDD (34.4%) groups in overall QOL satisfaction (79%), suggesting that mental health disorders, such as MDD, can significantly impact QOL (Table 2).

Table 2. Quality of life features (% Satisfaction) in study groups.

Aspect	Migraine (<i>n</i> = 60)	MDD (<i>n</i> = 64)	Control (<i>n</i> = 81)
Mobility	79.6	59.4	92.6
Positive Feelings	76.2	34.4	83.5
Self-esteem	79.7	37.5	77.8
Overall QOL	67.8	34.4	79.0
Safety	72.5	34.4	77.7
Home Environment	69.5	51.6	69.1
Work	67.8	37.5	77.8
Personal Relationships	69.5	42.2	65.0
Health and Social Care	65.6	65.6	64.2
Spirituality/Personal Beliefs	52.5	18.8	55.0
Overall Health	54.3	32.8	75.3
Body Image	64.2	39.6	65.0
Financial Resources	64.4	31.3	59.3
Sexual Activity	55.1	42.2	61.3
Social Support	61.0	42.2	59.3
Pain	35.6	29.7	11.1
Medication	42.4	37.5	6.2
Thinking and Concentration	37.3	17.2	59.2
Physical Environment	48.3	28.2	50.7
Energy	42.4	26.6	-
Leisure Activity	32.2	30.6	42.0
Sleep and Rest	33.9	40.7	48.1
Negative Feeling	49.2	59.3	23.5
ADLs (Activities of Daily Living)	37.3	23.4	-

Figure 3. Correlations and High-Risk Suicide Patterns in Study Groups. (A) Migraine group: correlation plots between suicide risk and quality of life. (B) MDD group: Correlation plots for suicide risk and quality of life. (C) Control group: Correlation plots between suicide risk and quality of life. (D) High-risk suicide proportions: The percentage of patients with a high suicide risk in the migraine, MDD, and control groups.



Gender, age, group classification, quality of life (QOL) score, and depression score were examined using univariate and multivariate regression models (Table 3). For gender, univariate analysis showed a non-significant positive association with the outcome (coefficient: .838, 95% CI: [-1.815, 3.491], $p = .534$), while multivariate analysis revealed a non-significant negative association (coefficient: -1.837, 95% CI: [-4.144, .470], $p = .118$). Similarly, age was not significant in either model, with coefficients of .041 (95% CI: [-.084, .166], $p = .519$) in the univariate model and .021 (95% CI: [-.089, .131], $p = .710$) in the multivariate analysis. In the group category, the MDD group had a non-significant negative association according to univariate analysis (coefficient: -1.302, 95% CI: [-4.584, 1.979], $p = .435$) and multivariate analysis (coefficient: -2.700, 95% CI: [-5.802, .402], $p = .088$), while the general group had a significant negative association according to univariate analysis (coefficient: -5.943, 95% CI: [-9.063, -2.823], $p < .001$) and a non-significant negative association according to multivariate analysis (coefficient: -2.441, 95% CI: [-5.413, .531], $p = .107$). The QOL score had a significant negative association according to the univariate model (coefficient: -.165, 95% CI: [-.256, -.075], $p < .001$) but showed a non-significant positive association according to the multivariate model (coefficient: .082, 95% CI: [-.025, .189], $p = .131$).

The depression score was significantly positive in both analyses (univariate coefficient=.720; 95% CI: [.569–.871]; $p < .001$; multivariate Coefficient =.826, 95% CI: [.621–1.031]; $p < .001$). Marital status, education, and occupation were included in the univariate model, but not in the multivariate model.

Table 3. Univariate and multivariate associations with the suicide risk rate.

Variable	Univariate Coefficient (95% CI)	<i>p</i> value	Multivariate Coefficient (95% CI)	<i>p</i> value
Gender	.838 ([-1.815, 3.491])	.534	-1.837 ([-4.144,.470])	.118
Age	.041 ([-.084,.166])	.519	.021 ([-.089,.131])	.710
Group				
MDD	-1.302 ([-4.584, 1.979])	.435	-2.700 ([-5.802,.402])	.088
General	-5.943 ([-9.063, -2.823])	<.001	-2.441 ([-5.413,.531])	.107
QOL Score	-.165 ([-.256, -.075])	<.001	.082 ([-.025,.189])	.131
Depression Score	.720 ([.569,.871])	<.001	.826 ([.621, 1.031])	<.001
Marital	.035 ([-2.655, 2.726])	.979	Not Included	
Education	-.658 ([-4.807, 3.491])	.755	Not Included	
Occupation	-2.004 ([-4.664,.655])	.139	Not Included	

DISCUSSION

The findings of this study provide valuable information regarding the interplay between sociodemographic factors, clinical characteristics, and mental health outcomes among individuals with migraine, MDD, and the general population. The significant differences in age and gender distributions observed align with previous findings indicating the prevalence of migraine and depressive disorders across different age groups and between genders [4, 29]. Studies have consistently shown that women are more prone to migraine and depression than men, which is reflected in our findings, with a greater proportion of women in the migraine and MDD groups [30-33].

The elevated depression scores observed in the migraine group (median PHQ-9: 11.0) and the remarkably similar suicide risk profiles between migraine and MDD groups provide compelling evidence supporting the well-established bidirectional relationship between migraine and affective disorders. This complex relationship represents one of the most extensively studied comorbidities in neuropsychiatry, with mounting evidence demonstrating that migraine and depression are not merely coincidental but share intricate pathophysiological mechanisms that create reciprocal causation patterns. The bidirectional nature of this relationship manifests through multiple pathways.

Migraine increases the risk of developing depression through several mechanisms: chronic pain-induced neuroplastic changes in pain processing circuits, disruption of sleep architecture leading to mood dysregulation, functional disability resulting in social isolation and reduced quality of life, and the psychological burden of living with an unpredictable, debilitating condition. Conversely, depression predisposes individuals to migraine development through altered serotonergic neurotransmission, hypothalamic-pituitary-adrenal axis dysfunction, increased inflammatory cytokine production, and maladaptive stress responses that lower migraine thresholds.

Neurobiologically, both conditions share common pathways involving serotonin dysregulation, altered GABA-ergic transmission, dysfunction in the trigeminovascular system, and abnormalities in the central pain processing networks including the periaqueductal gray, thalamus, and cortical pain matrix. The shared genetic susceptibility loci identified through genome-wide association studies further support the biological basis of this comorbidity. Longitudinal studies have consistently demonstrated that individuals with migraine have a 2.5-fold increased risk of developing depression, while those with depression have a 3.4-fold increased risk of developing migraine, establishing the temporal precedence that characterizes true bidirectional causation rather than simple association.

The clinical implications of this bidirectional relationship are profound, as comorbid migraine-depression presentations are associated with greater functional disability, increased healthcare utilization, poorer treatment response, and elevated suicide risk compared to either condition alone. The similar suicide risk profiles observed in our migraine and MDD groups (64.5 vs. 63.0 median scores) align with meta-analytic evidence demonstrating that comorbid migraine-depression confers the highest suicide risk among all migraine subtypes. Economic status, although not significantly different among our study groups, offers an interesting perspective when juxtaposed with existing research. Previous studies have demonstrated a link between lower socioeconomic status and an increased prevalence of mental health disorders, possibly due to increased stress and reduced access to healthcare services [1, 2, 34, 35]. Our findings suggest a similar trend, although the relationship is not as pronounced, indicating a need for further investigation. Substantial differences in occupational status and education levels between study groups echo the findings of previous studies that have highlighted the impact of educational attainment and employment status on mental health [36-38]. Unemployment and lower educational levels have been associated with increased stress and poorer health outcomes.

In terms of clinical characteristics, the significant differences in QOL and depression scores across the groups align with existing evidence [39,40]. It is well established that migraine and MDD can profoundly affect an individual's QOL [41,42]. The higher QOL scores observed in the migraine group than in the MDD group may be related to episodic migraines, allowing periods of respite compared to often-sustained depressive symptoms. This finding is consistent with the evidence of differential functional impacts across chronic conditions. When attacks occur, migraines can profoundly incapacitate their daily activities and strain their occupational duties, relationships, and academic performance. Persistent worry about the unpredictability of the next attack and its disruption of obligations can foster chronic anxiety and distress. This perpetual apprehension and uncertainty further diminish overall satisfaction and well-being in life. Ultimately, recurring uncertainty and functional impairment imposed by migraines appear to take a cumulative toll and steadily reduce QOL [43 – 45].

The negative correlation between QOL scores and suicide risk in the migraine group represents an important addition to research on the psychosocial burden of chronic pain [46, 47]. Migraine is associated with reduced productivity and enjoyment of life; therefore, this link to an elevated risk of suicide underscores the profound personal burden of the disease. Interestingly, the correlation between QOL and suicide risk was less significant in the MDD cohort. This finding suggests that depressive symptoms may be more predictive of suicide risk than QOL alone in this clinical population [40, 42, 46]. Our univariate models initially demonstrated statistically significant relationships between suicide risk and belonging to the general population, higher QOL, and increased depressive symptoms. However, multivariate analysis revealed a shift in which only the depression score remained a robust independent predictor after adjusting for confounders. Although migraine status did not confer a significantly greater risk than MDD, a comparison with the general population revealed a greater risk, again highlighting the relevance of chronic pain. However, when considering the full biopsychosocial picture, the severity of depression appeared to be the dominant driver of suicide risk. This exemplifies the complexity of mental health, as articulated in the foundational framework of Kessler et al. for psychiatric disorders [48,49].

Depression cannot be viewed in isolation from connected biological and external factors, such as pain or QOL. Ultimately, an integrative approach is imperative for suicide prevention and requires acknowledging multiple contributors in the biological, psychological, and social domains, even while targeting particular high-risk factors, such as severe depressive symptoms or migraines [46,50]. This approach will enable more personalized predictions and interventions to mitigate suicide risk in vulnerable groups.

Several potential sources of bias may have influenced the study results and warrant careful consideration in the interpretation of findings. Selection bias represents a primary concern, as the hospital-based recruitment strategy may have preferentially captured more severe cases of both migraine and MDD, potentially overestimating the strength of associations and limiting generalizability to community-based populations. The absence of population-based sampling introduces referral bias, as individuals seeking care at specialized headache clinics or psychiatric services may differ systematically from those managing their conditions in primary care or community settings. Information bias may have occurred through the reliance on self-reported questionnaires, which are susceptible to recall bias, social desirability bias, and varying levels of health literacy among participants.

The use of screening instruments rather than structured clinical interviews for psychiatric diagnosis introduces diagnostic bias, as these tools, while validated, were designed for screening rather than definitive diagnosis. The cross-sectional design inherently introduces temporal bias, precluding determination of causal relationships and the direction of associations between variables. Confounding bias represents another significant concern, as several unmeasured variables may have influenced the observed relationships.

These include medication effects (particularly prophylactic migraine medications and antidepressants), comorbid medical conditions (such as cardiovascular disease, diabetes, or other chronic pain conditions), family history of psychiatric disorders, genetic predisposition, cultural factors affecting symptom expression and help-seeking behavior, and socioeconomic variables beyond those captured in the study. The absence of systematic co-diagnosis assessment represents a critical methodological limitation that may have led to misclassification of participants and underestimation of the true burden of comorbid presentations.

Future research should address these limitations through several methodological improvements: (1) implementing population-based sampling strategies to enhance generalizability; (2) conducting longitudinal studies with multiple assessment points to establish temporal relationships and causal pathways; (3) incorporating structured clinical interviews alongside screening instruments to improve diagnostic accuracy; (4) systematically assessing for comorbid conditions across all participant groups; (5) collecting detailed medication histories and controlling for pharmacological effects; (6) including biomarker assessments to complement self-reported measures; (7) employing larger, more diverse samples to improve statistical power and external validity; and (8) utilizing advanced statistical techniques such as propensity score matching or instrumental variable analysis to address confounding. This study is strengthened by its inclusion of multiple mental health hospitals and a comparison group from the general population, bolstering the robustness of its conclusions.

The application of standardized Arabic translations of the WHOQOL-BREF and PHQ-9 instruments further reinforced the reliability of this study. The findings highlight the necessity for tailored interventions catering to distinct needs influenced by age, gender, economic status, and other individual characteristics. The associations and correlations observed lay the groundwork for future investigations, particularly in exploring the complex nature of mental health disorders and the differential impacts of sociodemographic factors in diverse cultural and geographical settings.

The limitations of this study have been extensively discussed above in the context of potential biases. Additionally, the cross-sectional design limits the capacity to establish causal links between variables and outcomes. Although diverse, the sample was relatively small and predominantly comprised Saudi nationals, which may constrain extrapolation of the findings to broader

populations. The exclusion of illiterate individuals and children also limits the representativeness of the sample. Participant discomfort in discussing certain QOL aspects, such as sexual health, further complicates the accuracy of data. The study's statistical power could be questioned due to multiple comparisons and complex models, raising concerns about type II errors. Nevertheless, these limitations underscore the importance of considering a broad spectrum of sociodemographic and clinical factors in the assessment and treatment of persons with migraine and MDD. This study also emphasizes the urgency for longitudinal research to unravel the temporal dynamics and causal relationships in the interplay between QOL, depression, and suicide risk across various populations.

CONCLUSION

This study revealed significant sociodemographic differences between Saudi adults with migraine or MDD and the general population. We observed a disproportionate burden of migraine among women, reflecting global patterns. Unemployment rates were also markedly higher in the clinical group, highlighting occupational status as an important factor. Clinically, the migraine cohort had the highest suicide risk scores and a significant negative correlation between QOL and suicidality, highlighting the psychological toll of migraine.

Our analyses identified associations between suicide risk and population groups, QOL, and severity of depression. Ultimately, these findings support customized interventions that respond to the sociocultural and clinical profiles of patients. Gender-conscious, culturally competent approaches are needed to address unequal burdens. Furthermore, the strong link between depression severity and suicidality requires coordinated screening and treatment to mitigate risk.

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