SHORT COMMUNICATION

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Quality of life and psychological comorbidities in patients with migraine and hypertension

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INTRODUCTION

Migraine is one of the most common headache subtypes and most affects the quality of life of the affected population and has several pathophysiological mechanisms that have not yet been appropriately clarified[1,2]. The relationship between migraine and systemic arterial hypertension (SAH) is causal to common risk factors such as family history, anxiety, and depression[3]. Also, neuropsychological comorbidities and sleep disturbances are factors that are intrinsically related to migraine and hypertension[4-6].

Evidence has suggested that stress may be a risk factor for SAH and exacerbating migraine symptoms[7,8]. Some studies further point to anxiety and depression being associated with migraine and hypertension[9-11]. However, these previous studies have not considered the effect of various confounding factors in analyzing the relationship between migraine and hypertension.

This study aimed to assess the occurrence and severity of psychological comorbidities (such as depression, anxiety, stress, and sleep disturbance) with migraine and SAH.

METHODS

This case-control study was conducted on outpatients of both sexes aged over 18 years, hypertensive, and non-hypertensive, with or without a diagnosis of migraine, screened at the University Hospital of Federal University of Maranhão, São Luís, Brazil, Maranhão, between December 2017 and July 2019. The research project was approved by the hospital's Research Ethics Committee (CAAE: 61420016.5.0000.5086). The participants were informed about the objectives and procedures involved in the study, and after indicating their complete understanding, they signed the informed consent form.

Patients diagnosed or had received treatment for any rheumatic, musculoskeletal, otorhinolaryngologic, malignant or benign neoplastic diseases, psychiatric disorder, had taken in the past 6 months or were taking anxiolytics, or any psychotropic or centrally acting analgesic, steroid, or alcohol and tobacco >15 days per month were excluded from this study.

The diagnosis of hypertension was made according to the American Heart Association criteria.

The General Health Questionnaire (GHQ-12) was used to evaluate the participants' general mental health condition, and The Depression, Anxiety and Stress Scale-21 (DASS-21) was used to evaluate depression, anxiety, and stress levels. The Pittsburg Sleep Quality Index (PSQI) was used to assess sleep quality. Patients were interviewed individually after recruitment to fill in the scales used.

The data were analyzed using SPSS version 28 (IBM, Chicago, Illinois, USA). Data related to descriptive analysis were expressed as percentages, means, standard deviation, medians, and interquartile ranges (IQR). The Kruskal-Wallis test was used to calculate the effect sizes (eta squared, η^2), followed by Dunn's multiple comparisons test for comparative analyses. Multiple linear regression was used to investigate the effect of migraine and hypertension on the psychometric scores, adjusted for age, sex, and body mass index. The D'Agostino-Pearson omnibus test was used to test the normality of residuals. A 5% significance level was adopted for all analyses.

RESULTS

In all, 124 patients were screened, and 54 were excluded based on eligibility criteria. A sample of 70 patients (47 females and

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23 males), with a mean age of 46.7±16.3 years, was included in this study. The frequency of migraine was 41.4% (Table 1). The assessment of Migraine Disability Assessment revealed that most patients had mild migraine (37.9%), and the median of this value was 7 (4–10). A value of 7 (3–12) was the median number of headache episodes in the last 3 months in patients with migraine.

The negative GHQ-12 showed significant differences between groups (p=0.001, effect size statistic η^2=0.190). The score was significantly higher in the migraine groups than in the nonmigraine group with hypertension (p<0.05). The DASS depression score was higher in the groups with migraine than in the groups without migraine and hypertension (p<0.05). The DASS anxiety score showed significant differences between groups (p<0.001, effect size statistic η^2=0.319). The migraine and hypertension group had higher anxiety scores than the other groups; in addition, the score of the group with migraine but without hypertension was higher than that of the group without both conditions. The DASS stress score was higher in the two groups with migraine than in the two groups without migraine. The PSQI score was not significantly different between the groups (p=0.124, effect size statistic η^2=0.042) (Table 2).

The adjusted effects of migraine and hypertension on psychometrics are shown in Table 3. The residuals of models 1, 3, and 4 showed an approximately normal distribution. Model 2 showed a significant departure from the normality assumption (statistics=5.234, p<0.001). The adjusted coefficients showed that migraine had a significant effect on the increment of GHQ-12 (beta=0.46, SE=0.12, p=0.001), DASS-21 anxiety score (beta=5.77, SE=1.07, p<0.001), and DASS-21 stress score (beta=8.18, SE=1.54, p<0.001).

DISCUSSION

Several studies have attempted to identify an association between migraine and hypertension[12-14]. However, none have been correlated with specific signs and symptoms associated with these comorbidities. Comparing patients with migraine and hypertension and those without migraine and hypertension, clear associations with psychological comorbidities could promote new therapeutic avenues for these diseases and, consequently, improve the quality of life of this population.

In this study, those with migraine in combination with SAH had higher levels of unfavorable overall health quality when compared to the group without migraine. This result corroborates that both migraine and SAH negatively influence the quality of life and, when associated, may further worsen it[14,15].

In the participants of this study, the presence of migraine, especially when combined with SAH, was accompanied by a higher frequency of depression and higher degrees of stress severity and anxiety symptoms. This relationship between depression and migraine is bidirectional, as shown by another study[16] based on a dose-response effect between migraine and depression and anxiety. The number of migraine attacks may increase the prevalence of mental disorders[4-7,17], due to the pathophysiological mechanisms involved, such as the attack on the serotonergic system, the influence of gonadotropins, and an increase in pro-inflammatory cytokines, and the presence of a family history[5].

Table 1. Comparative analysis on general health, neck pain, low back pain, depression, anxiety, stress, and sleep quality according to migraine and hypertension diagnosis.

	Migraine		No migraine		p-value
	Hypertension (n=9)	No hypertension (n=20)	Hypertension (n=21)	No hypertension (n=20)	
	Med (IQR)	Med (IQR)	Med (IQR)	Med (IQR)	
GHQ-12					
Positive score	2.1 (1.3–2.1)	2.0 (1.3–2.5)	1.8 (1.5–2.0)	1.6 (1.2–2.0)	0.522
Negative score	2.7 (1.3–2.1)[a]	2.0 (1.5–2.5)[a]	1.3 (1.1–1.5)[b]	1.5 (1.3–2.0)[a,b]	0.001
DASS-21					
Depression score	4 (2–6)[a]	2 (0–8)[a]	0 (0–2)[a,b]	0 (0–1)[b]	0.003
Anxiety score	14 (6–16)[a]	4 (2–8)[b]	2 (0–6)[b,c]	0 (0–2)[c]	<0.001
Stress score	14 (4–24)[a]	7 (4–16)[a]	2 (0–4)[b]	2 (0–3)[b]	<0.001
PSQI total score	2 (1–2)	2 (2–3)	2 (1–2)	2 (1–2)	0.124

Med: median; IQR: interquartile range (1st quartile – 3rd quartile); GHQ-12: general health questionnaire-12; DASS-21: depression, anxiety and stress scale-21; PSQI: Pittsburgh sleep quality index. After a Kruskal-Wallis test, different superscript letters indicate a significant difference by Dunn's multiple comparison post-test (p<0.05).

Stress is intrinsically related to SAH, and it can be both a risk factor and a consequence of this comorbidity[7], because there is an interconnection between these pathological pathways, with endothelial dysfunction being one of these elements, and stress may be a consequence or cause of an alteration in systemic blood pressure[17].

Moreover, studies show that stress has a bidirectional relationship with chronic migraine and may be a possible enhancer of other psychological comorbidities. In this context, serotonin is part of this association because it increases stress and participates in the central nucleus of pain, working as a pain stimulus[2,8].

Table 2. Multiple linear regression analysis of migraine and hypertension on health scores and salivary biomarkers levels.

Outcomes/factors	Multiple linear regression models[a]			
	R^2	Intercept	Beta	p-value
Outcome: GHQ-12 negative score	0.231	1.954		
Migraine			0.46	0.001*
Hypertension			-0.21	0.186
Outcome: DASS-21 depression	0.158	-0.622		
Migraine			3.54	0.002*
Hypertension			0.90	0.505
Outcome: DASS-21 anxiety	0.354	-2.581		
Migraine			5.74	<0.001*
Hypertension			3.36	0.014*
Outcome: DASS-21 stress	0.374	2.236		
Migraine			8.17	<0.001*
Hypertension			4.34	0.028*

R^2: determination coefficient; Beta: regression coefficient, GHQ-12: general health questionnaire-12; DASS-21: depression, anxiety and stress scale-21. [a]Multiple linear regression models adjusted by migraine, hypertension, age, female sex, and body mass index. *Statistically significant factor (p<0.05).

Table 3. Multiple linear regression analysis of migraine and hypertension on psychometric outcomes.

Outcomes/factors	Multiple linear regression models[a]				Normality of residuals of regression models	
	R^2	Beta	SE	p	Statistics	p
Model 1 Outcome: GHQ–12 Negative score	0.225				3.223	0.199
Migraine		0.46	0.12	0.001*		
Hypertension		-0.22	0.15	0.150		
Model 2 Outcome: DASS–21 depression	0.151				5.234	<0.001
Migraine		3.54	1.08	0.001*		
Hypertension		0.90	1.33	0.437		
Model 3 Outcome: DASS–21 anxiety	0.350				5.662	0.061
Migraine		5.77	1.07	<0.001*		
Hypertension		3.49	1.32	0.010*		
Model 4 Outcome: DASS–21 stress	0.374				3.566	0.168
Migraine		8.18	1.54	<0.001*		
Hypertension		4.40	1.89	0.023*		

R^2: determination coefficient; SE: standard error. Beta: regression coefficient. [a]Multiple linear regression models adjusted by migraine, hypertension, age, female sex and body mass index. *Statistically significant factor (p<0.05).

Serotonin is also present in physiopathological mechanisms related to poor-quality sleep. Experimental studies have demonstrated the association between serotonin, waking up at night, and migraine[18,19]. However, the results of those studies did not show differences between the groups. Relatedly, one study found that this causal relationship can reach a stage of stability when the frequency of headache attacks exceeds 9 days per month[20], which also occurred in most of our patients affected by migraine.

Some sleep disorders, such as obstructive sleep apnea and chronic insomnia, are associated with a higher risk of SAH[21-23]. However, research explained these associations with comorbidities such as obesity and depression, which are risk factors for increased blood pressure and poor sleep quality[24]. These confounding risk factors may have influenced the results related to SAH in the present study.

The study's limitations include the difficulty in finding individuals with SHA combined with migraine, since medications to treat hypertension end up helping to prevent migraine.

Patients with migraine had higher scores for overall negative health quality, anxiety, depression, and stress. Such scores were more evident in those with migraine and hypertension, although only anxiety had this combined effect statistically significant, demonstrating that these two conditions are more detrimental to physical and mental health.

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All procedures performed in studies involving human participants followed the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

The Ethics Committee of the Federal University of Maranhão approved the study (CAAE: 61420016.5.0000.5086).

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AUTHORS' CONTRIBUTIONS

TSR: Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **LSBA:** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **VPR:** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **CMBO**: Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **ECRM** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **LMMN:** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **LGLN**: Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **LVGM:** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **ECPPCL:** Conceptualization, Methodology, Formal Analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing.

REFERENCES

1. Shi X, Di W, Wieczorek A. Basic and clinical advances in the diagnosis and management of migraine. Pain Res Manag. 2020;2020:8958143. https://doi.org/10.1155/2020/8958143
2. Buse DC, Reed ML, Fanning KM, Bostic R, Dodick DW, Schwedt TJ, et al. Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: results of the migraine in America symptoms and treatment (MAST) study. J Headache Pain. 2020;21(1):23. https://doi.org/10.1186/s10194-020-1084-y
3. Hagen K, Stovner LJ, Zwart JA. Time trends of major headache diagnoses and predictive factors. Data from three Nord-Trøndelag health surveys. J Headache Pain. 2020;21(1):24. https://doi.org/10.1186/s10194-020-01095-5
4. Dresler T, Caratozzolo S, Guldolf K, Huhn JI, Loiacono C, Niiberg-Pikksööt T, et al. Understanding the nature of psychiatric comorbidity in migraine: a systematic review focused on interactions and treatment implications. J Headache Pain. 2019;20(1):51. https://doi.org/10.1186/s10194-019-0988-x
5. Maatouk I, Herzog W, Böhlen F, Quinzler R, Löwe B, Saum KU, et al. Association of hypertension with depression and generalized anxiety symptoms in a large population-based sample of older adults. J Hypertens. 2016;34(9):1711-20. https://doi.org/10.1097/HJH.0000000000001006
6. Dich N, Rod NH, Doan SN. Both High and Low Levels of Negative Emotions Are Associated with Higher Blood Pressure: Evidence from Whitehall II Cohort Study. Int J Behav Med. 2020;27(2):170-8. https://doi.org/10.1007/s12529-019-09844-w

7. Liu MY, Li N, Li WA, Khan H. Association between psychosocial stress and hypertension: a systematic review and meta-analysis. Neurol Res. 2017;39(6):573-80. https://doi.org/10.1080/01616412.2017.1317904
8. Cha MJ, Kim BK, Moon HS, Ahn JY, Oh K, Kim JY, et al. Stress is associated with poor outcome of acute treatment for chronic migraine: a multicenter study. Pain Med. 2018;19(9):1832-8. https://doi.org/10.1093/pm/pnx269
9. Bougea A, Spantideas N, Galanis P, Katsika P, Boufidou F, Voskou P, et al. Salivary inflammatory markers in tension type headache and migraine: the SalHead cohort study. Neurol Sci. 2020;41(4):877-84. https://doi.org/10.1007/s10072-019-04151-4
10. Peres MFP, Mercante JPP, Tobo PR, Kamei H, Bigal ME. Anxiety and depression symptoms and migraine: a symptom-based approach research. J Headache Pain. 2017;18(1):37. https://doi.org/10.1186/s10194-017-0742-1
11. Gray CA, Sims OT, Oh H. Prevalence and predictors of co-occurring hypertension and depression among community-dwelling older adults. J Racial Ethn Health Disparities. 2020;7(2):365-73. https://doi.org/10.1007/s40615-019-00665-x
12. Gudmundsson LS, Thorgeirsson G, Sigfusson N, Sigvaldason H, Johannsson M. Migraine patients have lower systolic but higher diastolic blood pressure compared with controls in a population-based study of 21,537 subjects. The Reykjavik Study. Cephalalgia. 2006;26(4):436-44. https://doi.org/10.1111/j.1468-2982.2005.01057.x
13. Lima GS, Laurentino IMS, Silva VNC, Leite AFB, Valença MM, Santos ERR. Interactive between headache, systemic arterial hypertension and stoke: a integrative review. HM [Internet]. 2018;9(4):199-204. https://doi.org/10.48208/HeadacheMed.2018.23
14. Burch RC, Buse DC, Lipton RB. Migraine: Epidemiology, burden, and comorbidity. Neurol Clin. 2019;37(4):631-49. https://doi.org/10.1016/j.ncl.2019.06.001
15. Plesh O, Adams SH, Gansky SA. Self-reported comorbid pains in severe headaches or migraines in a US national sample. Headache. 2012;52(6):946-56.https://doi.org/10.1111/j.1526-4610.2012.02155.x
16. Breslau N, Davis GC, Schultz LR, Paterson EL. Migraine and major depression: a longitudinal study. Headache. 1994;34(7):387-93. https://doi.org/10.1111/j.1526-4610.1994.hed3407387.x
17. Vgontzas A, Pavlović JM. Sleep Disorders and Migraine: Review of Literature and Potential Pathophysiology Mechanisms. Headache. 2018;58(7):1030-9. https://doi.org/10.1111/head.13358
18. Ushakov AV, Ivanchenko VS, Gagarina AA. Psychological stress in pathogenesis of essential hypertension. Curr Hypertens Rev. 2016;12(3):203-14.https://doi.org/10.2174/1573402112666161230121622
19. Ferini-Strambi L, Galbiati A, Combi R. Sleep disorder-related headaches. Neurol Sci. 2019;40(Suppl 1):107-13. https://doi.org/10.1007/s10072-019-03837-z
20. Buse DC, Rains JC, Pavlovic JM, Fanning KM, Reed ML, Manack Adams A, et al. Sleep disorders among people with migraine: results from the chronic migraine epidemiology and outcomes (CaMEO) study. Headache. 2019;59(1):32-45. https://doi.org/10.1111/head.13435
21. Hein M, Lanquart JP, Loas G, Hubain P, Linkowski P. Risk of high blood pressure associated with objective insomnia and self-reported insomnia complaints in major depression: a study on 703 individuals. Clin Exp Hypertens. 2019;41(6):538-47. https://doi.org/10.1080/10641963.2018.1516775
22. Jarrin DC, Alvaro PK, Bouchard MA, Jarrin SD, Drake CL, Morin CM. Insomnia and hypertension: a systematic review. Sleep Med Rev. 2018;41:3-38. https://doi.org/10.1016/j.smrv.2018.02.003
23. Carnethon MR, Johnson DA. Sleep and Resistant Hypertension. Curr Hypertens Rep. 2019;21(5):34. https://doi.org/10.1007/s11906-019-0941-z
24. Mansukhani MP, Covassin N, Somers VK. Apneic sleep, insufficient sleep, and hypertension. Hypertension. 2019;73(4):744-56. https://doi.org/10.1161/HYPERTENSIONAHA.118.11780