

RESEARCH

Open Access



Association between severe headache or migraine and lipid accumulation product and visceral adiposity index in adults: a cross-sectional study from NHANES

Caixiang Zhuang^{1†}, Jiesheng Mao^{1†}, Hongyu Ye¹, Jianghai He¹, Yuwen Hu¹, Haoxiang Hu¹ and Yanyan Zheng^{1*}

Abstract

Background Existing literature on the impact of lipid accumulation product (LAP) and visceral adiposity index (VAI) on severe headache or migraine is limited. This study aims to elucidate the association between LAP and VAI and the prevalence of migraine.

Methods Data for this study were sourced from the 1999–2004 National Health and Nutrition Examination Survey (NHANES). A database-self-administered questionnaire was used to assess severe headache or migraine. A weighted logistic regression model was employed to assess the relationship between LAP and VAI with migraine prevalence. Complementary analytical approaches included subgroup analysis, restricted cubic spline (RCS), and threshold effect analysis to validate the findings.

Results In the end, 4572 people were recruited for the research, including 880 with migraine and 3692 without migraine. Following adjustment for the relevant covariables, weighted logistic regression analysis (OR = 1.409, 95% CI: 1.054, 1.883, $P = 0.022$; OR = 1.288, 95% CI: 1.010, 1.642, $P = 0.042$) revealed significantly elevated odds of migraine prevalence in participants within the highest tertile (T3) of LAP and VAI than those in the lowest tertile (T1). The nonlinear association between migraine prevalence and both VAI and LAP was further elucidated through a restricted cubic spline. The threshold analysis pinpointed 2.142 (log-likelihood ratio = 0.016) as the critical inflection point for VAI. Subgroup analysis and interaction testing revealed the significant association was independent in different subgroup factors.

Conclusions The data indicate a robust association between higher levels of LAP and VAI and an increased prevalence of migraine.

[†]Caixiang Zhuang and Jiesheng Mao contributed equally to this work.

*Correspondence:

Yanyan Zheng
Yying33171@163.com

¹Department of Neurology, Postgraduate Training Base Alliance of Wenzhou Medical University (Wenzhou People's Hospital), Wenzhou, China



Introduction

Migraine, a severe and debilitating neurovascular disorder, has an immense impact on people's lives and society [1]. This condition manifests as frequent, unilateral, pulsating, intense headaches in addition to nausea, vomiting, and heightened sensitivity to light and sound [2]. Research highlights that migraines are the predominant cause of disabilities in persons under 50, significantly affecting life expectancy post-disability [3]. In the USA, 15% of adults suffer from a migraine attack annually, with the global burden reaching approximately 1 billion affected individuals [4]. Understanding modifiable determinants for migraine is crucial for reducing its associated morbidity, given the significant cost that migraines cause to people in the world. Researchers have looked into the potential linkage between migraine and obesity-related metrics in the past several years [5, 6], thus underscoring the relevance of further research into the effects of obesity on migraine.

Accumulation of visceral fat is a hallmark of obesity. However, traditional metrics, such as body mass index (BMI), fail to distinguish between subcutaneous and visceral fat, thereby limiting their effectiveness in assessing obesity severity. VAI represents an innovative anthropometric measure useful for evaluating the function and distribution of visceral fat [7]. VAI is determined by integrating BMI, waist circumference (WC), triglyceride (TG), and high-density lipoprotein (HDL) cholesterol via a specific mathematical Eq. [8]. Another tool for determining and displaying the state of fat accumulation is LAP, which is derived by amalgamating WC and TG. Based on clinical research, VAI and LAP have demonstrated their ability to accurately identify those who are more susceptible to metabolic disorders linked to visceral obesity, such as abnormalities in lipids, insulin resistance, and cardiovascular detrimental factors [9–12]. These indices have also shown superior predictive accuracy in some clinical circumstances [13, 14], outperforming more conventional measures such as waist-height ratio and body mass index [15, 16]. However, research exploring the potential relationship between VAI, LAP, and migraine remains scarce. Elucidating this relationship could be useful in the proposal of tailored tactics to mitigate the detrimental effects of migraine on public health.

The research used statistics from the NHANES to perform the cross-sectional analysis of the relationship examining the impact of LAP and VAI, on migraine prevalence, positing a high influence of these indices on migraine occurrence.

Methods

Study population

NHANES, a multistage, stratified, nationally representative probability sample survey [17], aims to assess the

association between disease prevention and nutritional practices for health enhancement. Conducted biennially, this survey integrates interviews with physical examinations and encompasses demographic, nutritional, examination, laboratory, and questionnaire components.

This study used the 1999–2004 NHANES as only this cycle's data, as they included data pertinent to reported headaches and migraines. 19,063 of the 31,126 participants who were initially included in the study were removed due to missing data on BMI, income-to-poverty ratio (PIR), educational attainment, alcohol intake, marital status, and smoking status. Further exclusions were made for missing data on diabetes, hyperlipidemia, and hypertension (1,415 participants), and incomplete information on migraine, TG, WC, TC, HDL-C, and low-density lipoprotein cholesterol (LDL-C) (6,076 participants). Participants younger than 20 years were excluded, leaving a final sample size of 4,572 people (Fig. 1).

Definition of LAP and VAI

The LAP and VAI are sex-specific indices that estimate abdominal lipid accumulation and assess visceral adiposity functionality respectively. The formulas below were employed to compute each participant's LAP and VAI based on previous studies, where TG and HDL-C were in mmol/L, and WC was in cm [8, 15].

$$\text{For males: } LAP = (WC - 65) * TG$$

$$VAI = WC^{(39.68 + 1.88 * BMI)} * (TG^{1.03}) * (1.31/HDL_C)$$

$$\text{For females: } LAP = (WC - 58) * TG$$

$$VAI = WC^{(36.58 + 1.89 * BMI)} * (TG^{0.81}) * (1.52/HDL_C)$$

Definition of severe headache or migraine

The Pain Questionnaire was the primary tool used to ascertain the status of migraine, following methodologies consistent with prior NHANES-based study techniques [18]. A positive response to the question, "In the past three months, have you experienced a severe headache or migraine?" defined participants with a severe headache or migraine.

Selection of covariables

The analysis incorporated potential confounding variables associated with LAP, VAI, and migraine based on prior research [18, 19]. These variables included age (year), gender (male/female), race (Mexican American / non-Hispanic White/non-Hispanic Black/other races), education attainment (less than high school/high school/above high school), marital status (divorced/married/never married), total cholesterol levels (mmol/L), PIR, BMI (kg/m²), diabetes (yes/no), hyperlipidemia (yes/no),

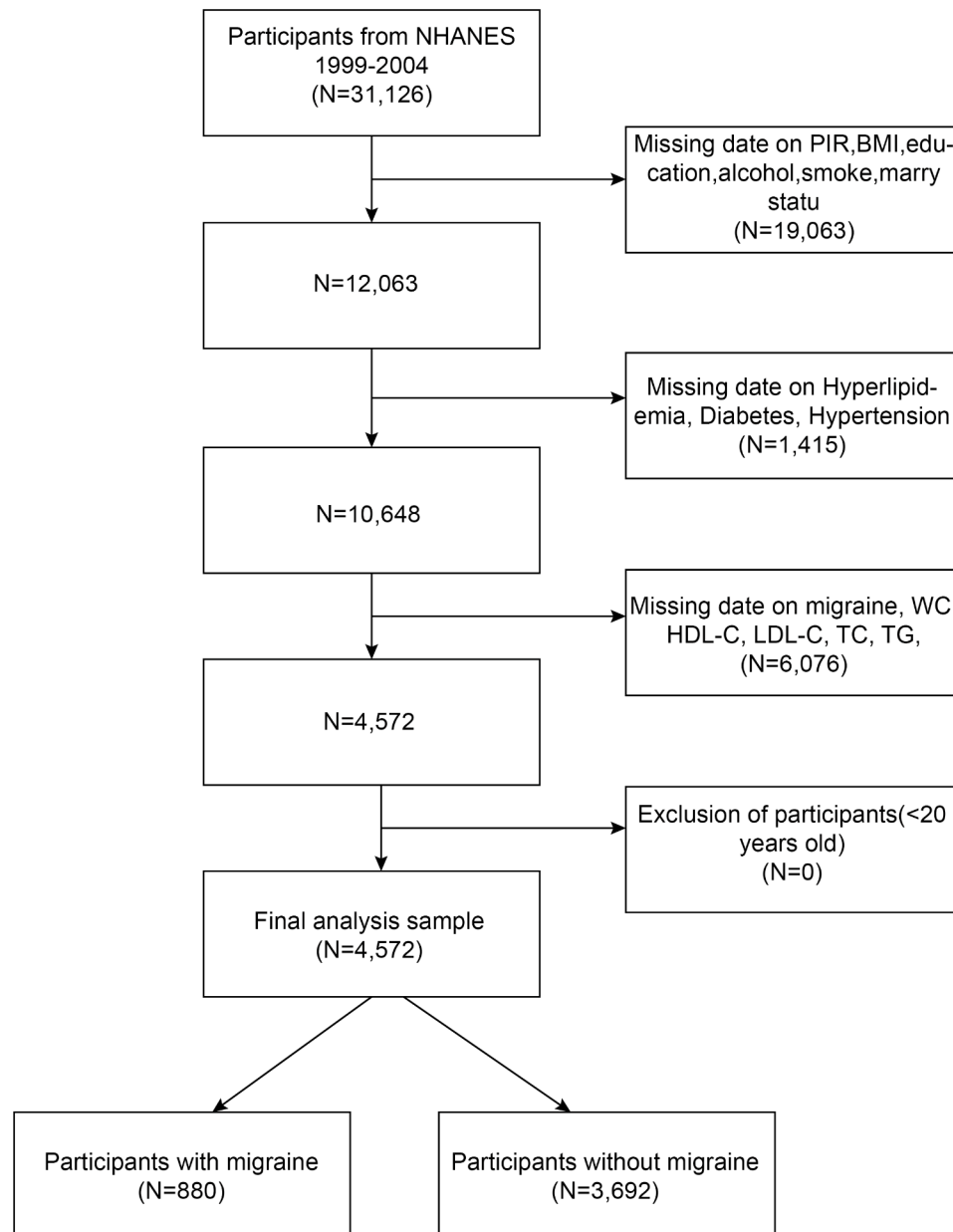


Fig. 1 Flow chart of participants selection

and hypertension(yes/no) were all included. The categories for smoking status were never, ever, and currently smoking. Alcohol consumption was defined as “never”, “mild”, “moderate”, “heavy”, and “former”. You may get more details at <http://www.cdc.gov/nhanes>.

Statistical analysis

Continuous variables included age, PIR, BMI, waist circumference, TG, LDL-C, HDL-C, TC, VAI, and LAP. Categorical variables included age group, gender, race, marry status, education level, smoking status, alcohol consumption, hypertension (yes/no), diabetes (yes/no), and hyperlipidemia (yes/no). Weighted chi-square tests

and weighted t-tests were used for categorical variables and continuous variables respectively, and Mann-Whitney U test was used for non-normally distributed continuous variables in statistical analyses stratified by migraine to evaluate baseline participant characteristics. Three distinct models of weighted multiple logistic regression were utilized to elucidate the relationships between VAI, LAP, and migraine. Model 1 was unadjusted. Age, gender, and racial adjustments were incorporated into Model 2. Model 3 received adjustments for marital status, educational level, income-to-poverty ratio, hypertension, hyperlipidemia, alcohol consumption, and smoking status building upon the framework established in Model

2. The authors employed trend tests to investigate linear patterns in the relationship between the VAI, LAP, and migraine, after categorizing VAI and LAP to categorical variables (tertiles). Subgroup analyses respectively performed analyzed the associations between LAP, VAI, and migraine in populations with varying demographics, including age, gender, race, educational level, and hypertension. Interaction tests were executed to determine if the relationships were consistent across all subgroups. The non-linear associations were assessed using restricted sample cubic spline (RCS) analysis between VAI, LAP, and migraine. The RCS analysis was conducted using 3 knots located at the 10th, 50th, and 90th percentiles. Two-sided $P < 0.05$ was considered to have statistical relevance. EmpowerStats (version 2.0) and R (version 4.2.2) served as the foundation for analyses.

Results

Baseline characteristic

The study included 4,572 people who satisfied the inclusion criteria. It shows details of individuals segmented by migraine presence or absence, with 880 individuals identified in the migraine group in Table 1. Participants were 46.35 (0.47) years old on average, with females representing 50.63% and males 49.37%. The Median (Q1-Q3) of VAI and LAP were 1.69 (1.03–2.74) and 43.12 (23.67–71.65), respectively. The migraine group exhibited significantly higher VAI values than the non-migraine group. Furthermore, significant variations in age, gender, education, smoking, LAP, PIR, and BMI were observed between the two groups.

Association between VAI, LAP and migraine

In Table 2, with VAI and LAP reclassified into tertiles, it demonstrated that individuals in the highest tertile for VAI and LAP, as per the adjusted Model 3, had increased odds of 40.9% and 28.8% for migraine prevalence, respectively, compared to the lowest tertile (OR=1.409, 95% CI: 1.054, 1.883, $P=0.022$; OR=1.288, 95% CI: 1.010, 1.642, $P=0.042$).

The restricted cubic spline in Fig. 2 showed a nonlinear association between LAP (P nonlinear=0.046) and VAI (P nonlinear=0.0023) with migraine. Threshold analysis identified an inflection point for VAI at 2.142 (log-likelihood ratio=0.016), as shown in Table 3. Below this inflection point, it indicates that the prevalence of migraine increases with higher levels of VAI. Above this level, the association between increased VAI and migraine dissipated, indicating that further rises in VAI did not substantially augment the prevalence of migraine.

Subgroup analyses

Subgroup analysis detailed in Table 4 considered age, gender, BMI, and hypertension. The results showed

a consistent association across subgroups between migraine and VAI, LAP. Although females aged 20–39 demonstrated a stronger positive association between LAP and migraine, the interaction effects were not statistically significant (Age: P interaction=0.09; Gender: P interaction=0.985).

Discussion

The study establishes a positive association between migraine, VAI, and LAP in a cross-sectional analysis, suggesting that increased levels of VAI or LAP are linked to an elevated prevalence of migraine. Significantly, non-linear associations between LAP and VAI with migraine were observed, and the VAI's inflection point (2.142) was pinpointed. Additionally, no significant effect was noted after taking into account age, gender, BMI, and hypertension. These findings underscore the potential of fat reduction and visceral fat control in mitigating migraine prevalence.

This investigation is possibly the inaugural study examining the association between LAP, VAI, with migraine. Between 2003 and 2004, a prospective, 11-month population-based follow-up study conducted in the United States suggested a link between migraine and obesity [20]. Compared to those of normal weight, participants with elevated BMIs experienced a higher relative prevalence of chronic migraine. A study of observation conducted in Iran found that migraineurs with higher BMI had more frequent, severe, and prolonged headaches, alongside higher disability scores [21]. In comparison to those of normal weight, Meta-analyses have similarly reported a 14% and 27% increased prevalence of migraine in obese individuals [22, 23]. Kristoffersen et al. found that adipose tissue distribution may influence the impact of obesity on the occurrence of migraine [24]. Blood lipoprotein is one of the important indicators for calculating VAI and LAP. Multiple observational studies have posited a possible association between dyslipidemia with other aspects in migraine, including intensity, occurrence, as well as frequency [25–27]. Additionally, there is recent evidence that statins may reduce the likelihood of migraine [28] and metabolic disorders such as obesity may affect the efficacy of migraine medications [29]. Previous studies have found that blood lipoprotein subfractions and migraine were caused by shared hereditary causes [30, 31]. However, these studies did not further investigate the role of visceral fat on migraine. Thus, NHANES provides a unique opportunity to confirm if VAI, LAP, and migraine are positively correlated, which will lay the groundwork for further research into the impact of obesity on migraine.

While the precise mechanisms linking VAI, LAP, and migraine remain elusive, there are multiple possible explanations. Firstly, visceral obesity, a particularly

Table 1 Baseline characteristics of whether the participants with migraine

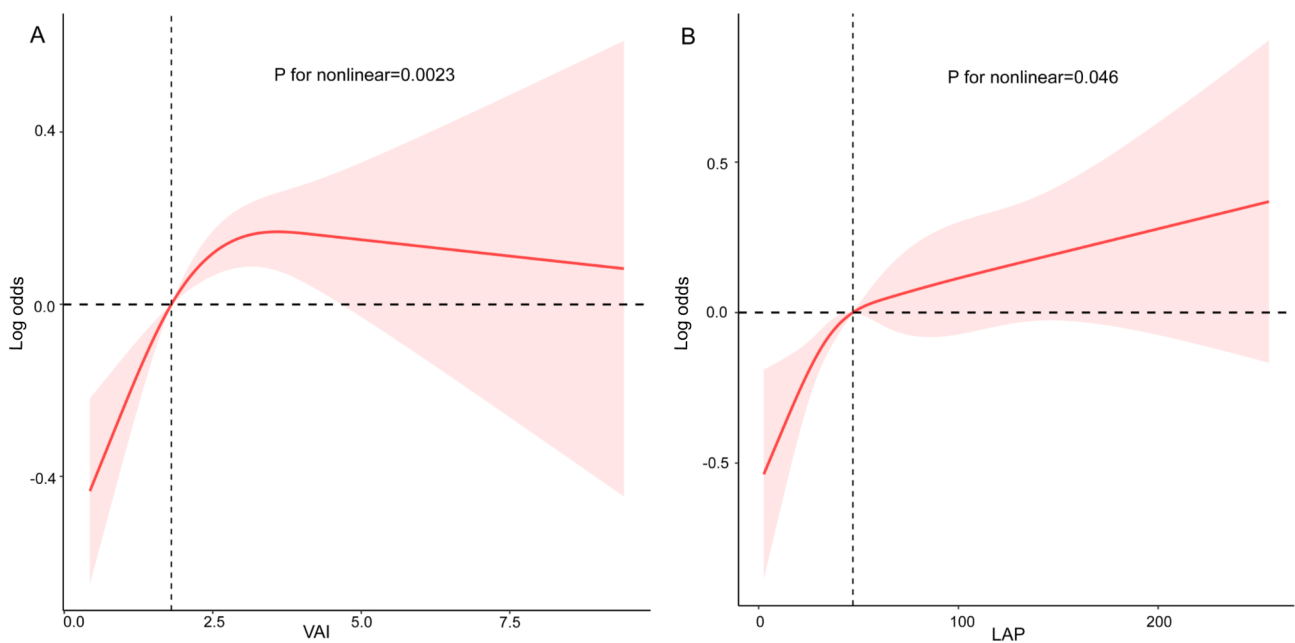
Variable	Total (N=4572)	Migraine (N=880)	Control (N=3692)	P-value
Age(years)	46.35 ± 0.47	42.72 ± 0.41	47.32 ± 0.57	< 0.0001
Age group, (%)				< 0.0001
20–39	38.27(0.02)	43.28(1.62)	36.92(1.49)	
40–59	39.55(0.02)	45.66(1.51)	37.91(0.96)	
≥ 60	22.18(0.01)	11.06(1.05)	25.16(1.16)	
Gender, (%)				< 0.0001
Female	50.63(0.02)	63.68(1.74)	47.13(0.70)	
Male	49.37(0.02)	36.32(1.74)	52.87(0.70)	
Race, (%)				0.13
Mexican American	6.99(0.01)	7.98(1.47)	6.72(0.88)	
Non-Hispanic Black	9.58(0.01)	10.06(1.41)	9.45(1.08)	
Non-Hispanic White	74.43(0.05)	71.03(2.60)	75.34(1.91)	
Other Race	9.00(0.01)	10.92(2.11)	8.49(1.30)	
PIR	3.09 ± 0.06	2.72 ± 0.07	3.19 ± 0.06	< 0.0001
Marry status, (%)				0.1
Divorced/Widowed/Separated	17.31(0.01)	16.67(1.27)	17.48(0.88)	
Married/Living with partner	67.49(0.03)	70.17(1.53)	66.77(1.25)	
Never married	15.20(0.01)	13.16(1.37)	15.75(1.03)	
Education level, (%)				< 0.001
< high school	18.83(0.01)	23.71(1.24)	17.51(0.92)	
=high school	26.48(0.02)	28.54(1.91)	25.93(1.22)	
> high school	54.70(0.02)	47.75(2.26)	56.56(1.44)	
Smoking status, (%)				0.001
former	26.49(0.02)	22.40(1.82)	27.59(1.19)	
never	49.19(0.02)	47.40(2.60)	49.67(1.29)	
now	24.32(0.02)	30.20(2.37)	22.74(1.05)	
Alcohol user, (%)				0.24
former	17.21(0.02)	18.94(1.69)	16.74(1.12)	
heavy	19.71(0.01)	20.74(1.87)	19.44(0.95)	
mild	35.99(0.02)	33.35(1.82)	36.70(1.36)	
moderate	16.14(0.01)	14.73(1.74)	16.52(0.86)	
never	10.95(0.01)	12.25(1.63)	10.60(1.25)	
Hypertension, (%)				0.32
No	64.23(0.03)	65.61(1.62)	63.86(1.13)	
Yes	35.77(0.02)	34.39(1.62)	36.14(1.13)	
Hyperlipidemia, (%)				0.68
No	25.89(0.01)	26.53(1.84)	25.72(0.94)	
Yes	74.11(0.03)	73.47(1.84)	74.28(0.94)	
Diabetes, (%)				0.99
No	94.11(0.04)	94.09(0.79)	94.11(0.50)	
Yes	5.89(0.01)	5.91(0.79)	5.89(0.50)	
BMI, (kg/m ²)	28.01 ± 0.13	28.71 ± 0.26	27.83 ± 0.15	0.004
Waist Circumference (cm)	96.34 ± 0.34	96.51 ± 0.69	96.30 ± 0.37	0.78
TG(mmol/L)	1.38 ± 0.02	1.39 ± 0.03	1.37 ± 0.02	0.51
LDL-C (mmol/L)	3.13 ± 0.02	3.08 ± 0.04	3.15 ± 0.02	0.13
HDL-C (mmol/L)	1.36 ± 0.01	1.34 ± 0.02	1.36 ± 0.01	0.16
TC(mmol/L)	5.12 ± 0.02	5.07 ± 0.04	5.14 ± 0.02	0.11
VAI, Median(Q1-Q3)	1.69(1.03–2.74)	1.82(1.10–2.80)	1.66(1.02–2.71)	0.03
LAP, Median(Q1-Q3)	43.12 (23.67–71.65)	43.94(23.58–73.30)	42.92(23.80–71.33)	0.32

Abbreviation: PIR: income-to-poverty ratio; BMI: body mass index; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VAI: Visceral adiposity index; LAP: Lipid accumulation product

Table 2 Multivariable logistic regression models for the association between LAP, VAI, and migraine in adults in the NHANES

Migraine	OR (95% CI), P-value		
	Model 1	Model 2	Model 3
VAI			
Tertile 1 (≤ 1.225)	Reference	Reference	Reference
Tertile 2 (1.225–2.275)	1.189(0.918,1.541), 0.185	1.273(0.988,1.641), 0.062	1.246(0.938,1.656), 0.124
Tertile 3 (> 2.275)	1.315(1.027,1.682), 0.031	1.524(1.193,1.946), 0.001	1.409(1.054,1.883), 0.022
P for tend	0.038	0.002	0.029
LAP			
Tertile 1 (≤ 32.501)	Reference	Reference	Reference
Tertile 2 (32.501–65.582)	1.021(0.803,1.300), 0.861	1.301(1.023,1.655), 0.033	1.254(0.952,1.651), 0.103
Tertile 3 (> 65.582)	1.052(0.881,1.257), 0.567	1.411(1.162,1.715), < 0.001	1.288(1.010,1.642), 0.042
P for tend	0.566	< 0.001	0.041

Abbreviations: VAI: Visceral adiposity index; LAP: Lipid accumulation product; NHANES: National Health and Nutrition Examination Survey; OR: odds ratio; CI: confidence interval

**Fig. 2** The restricted cubic spline (RCS) analysis between VAI and LAP with migraine

deleterious form of central obesity, is well-represented by VAI or LAP, which signifies both visceral fat accumulation and functional metabolic disturbances. Generally speaking, obesity is commonly characterized as a systemic inflammatory condition, marked by elevated levels of pro-inflammatory cytokines, including interleukin (IL)-1, IL-6, and tumor necrosis factor- α (TNF- α) [32, 33]. As an endocrine organ, fat tissue is known to generate pro-inflammatory adipocytokines, such as lipocalin and leptin [34, 35]. Additionally, it is posited that increased leptin levels trigger the release of NO as well as pro-inflammatory proteins, such as TNF- α and IL-6, implicated in migraine pathogenesis via the nuclear factor- κ B signaling pathway [36]. Indeed, migraineurs exhibit higher levels of pro-inflammatory markers and adipocytokines [37–40]. Perini et al. suggested that

inflammation could be a key pathogenic mechanism for migraine [41]. Calcitonin gene-related peptide (CGRP), a crucial neurobiological mediator, is another plausible explanation behind the link between fat and migraine. It is believed that CGRP controls how pain signals are transmitted throughout the brain and may have a role in the perception of meningeal injury [42]. Elevated CGRP levels have been observed in both obese individuals and those with migraine compared to their non-obese and non-migraine counterparts [43, 44]. According to Ligong et al., noted that inflammatory peptides could cause irreversible damage to the perithalamic gray matter and sensitize the central nervous system, all of which are linked to the pathogenesis of migraine [45].

Evidence suggests that patients with chronic migraine exhibit elevated levels of orexin in their cerebrospinal

Table 3 Threshold effect analysis of LAP and VAI on migraine using a two-piecewise logistic regression model in adults in the NHANES

Threshold effect analysis	Migraine OR (95%CI)
VAI	
The inflection point of VAI (K)	2.142
< K slope	1.290 (1.082, 1.539)
> K slope	0.992 (0.922, 1.067)
Log-likelihood ratio test	0.016
LAP	
The inflection point of LAP (K)	46.252
< K slope	1.008 (1.001, 1.015)
> K slope	1.001 (0.999, 1.004)
Log-likelihood ratio test	0.122

Abbreviation: VAI: Visceral adiposity index.; LAP: Lipid accumulation product; NHANES: National Health and Nutrition Examination Survey;

Notes: The analysis was based on Model 3

fluid [46]. These heightened orexin levels not only induce hyperphagia [47] but also exacerbate mitochondrial dysfunction [48], contributing to the development of obesity [49]. Furthermore, the results of a macrogenome-wide association study have revealed that migraineurs exhibit significantly reduced microbial diversity and altered metabolic functions within their gut microbiota compared to healthy controls [50]. This dysbiosis disrupts host energy homeostasis, induces low-grade chronic inflammation through the impairment of intestinal barrier integrity, and elevates the expression of hunger-suppressing hormones, ultimately leading to obesity [51, 52]. The disabling nature of migraine often impedes regular physical activity among affected individuals [53], which is a critical factor in weight management. Additionally,

migraineurs are at a markedly increased likelihood of developing depression and anxiety disorders [54, 55]. These psychiatric conditions are themselves associated with obesity and significant weight gain [56]. This bidirectional relationship between migraine and obesity creates a vicious cycle where one condition exacerbates the other. The complexity of this relationship is further compounded by shared detrimental factors, including genetic predispositions, physical inactivity lifestyle, and poor dietary habits [57].

Study strengths and limitations

There are some strengths in this study. Firstly, NHANES is an important epidemiological study conducted in the United States. Strict quality control processes are used in the data collection process, and the results are highly dependable. In addition, findings were further reinforced by adjusting for confounding factors through subgroup analysis.

However, the study's limitations are notable. First, the reliance on self-reported data to determine the presence of severe headache or migraine could introduce recall bias. Second, there might be factors that were not taken into account, even if have eliminated extensive adjustments for confounding variables. Furthermore, causal inference is limited by the cross-sectional nature of this study.

Conclusions

In conclusion, the research shows higher levels of VAI or LAP are independently associated with an increased prevalence of migraine, underscoring their potential as predictive biomarkers. Modulating VAI and LAP levels

Table 4 Stratified analysis of the association between LAP, VAI and migraine in adults in the NHANES

Subgroup	OR (95% CI)		P interaction
	VAI	LAP	
Age			0.823
20–39	1.008(0.918,1.106)	1.004(1.001,1.007)	
40–59	1.095(0.982,1.221)	1.002(0.998,1.006)	
> 60	1.024(0.862,1.217)	0.999(0.992,1.006)	
Gender			0.877
Male	1.067(0.952,1.195)	1.003(0.999,1.006)	
Female	1.068(0.994,1.149)	1.003(1.000,1.007)	
BMI			0.452
< 25	0.987(0.872,1.118)	0.999(0.990,1.007)	
25–30	1.116(0.999,1.246)	1.002(0.997,1.008)	
> 30	1.028(0.912,1.160)	1.003(0.999,1.006)	
Hypertension			0.664
Yes	1.072(0.952,1.207)	1.003(0.999,1.007)	
No	1.052(0.968,1.145)	1.003(1.000,1.006)	

Abbreviation: VAI: Visceral adiposity index; LAP: Lipid accumulation product; NHANES: National Health and Nutrition Examination Survey; OR: odds ratio; CI: confidence interval

Note: Age, gender, race, education level, marital status, poverty income ratio, hypertension, hyperlipidemia, alcohol use, and smoking status were adjusted. The strata variable was not included in the model when stratifying by itself

may serve as a prophylactic measure and help mitigate migraine progression. For people with high VAI and LAP levels, dietary modifications and exercise regimens as medical interventions are advised to reduce the prevalence of migraine. The results underscore the significance of using VAI and LAP measurements in clinical assessments to direct focused interventions and enhance outcomes in individuals with a higher prevalence of migraine.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12944-024-02303-w>.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

We appreciate the National Center for Health Statistics of the Centers for Disease Control staff for collecting the NHANES data and creating the public database.

Author contributions

C.Z. and J.M. wrote the main manuscript text and H.Y. prepared Figs. 1 and 2. J.H. and Y.H. prepared Tables 1, 2, 3 and 4. Y.Z. and H.H. were responsible for instructional writing and data analysis. All authors reviewed the manuscript.

Funding

The paper was not funded.

Data availability

This study examines data that is available to the public. You may get the complete set of data at <https://www.cdc.gov/nchs/nhanes/index.htm>.

Declarations

Ethics approval

The datasets were obtained from the NHANES database, and all data were under ethics approval before recorded in the database.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 10 August 2024 / Accepted: 16 September 2024

Published online: 27 September 2024

References

1. Waliszewska-Prosoń M, Montisano DA, Antolak M, Bighiani F, Cammarota F, Cetta I, Corrado M, Ihara K, Kartamysheva R, Petrušić I, et al. The impact of primary headaches on disability outcomes: a literature review and meta-analysis to inform future iterations of the Global Burden of Disease study. *J Headache Pain*. 2024;25:27.
2. Classification. Diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Headache Classif Comm Int Headache Soc Cephalalgia*. 1988;8(Suppl 7):1–96.
3. Steiner TJ, Husøy A, Stovner LJ. GBD2021: headache disorders and global lost health - a focus on children, and a view forward. *J Headache Pain*. 2024;25:91.
4. Zhang N, Robbins MS. Migraine. *Ann Intern Med*. 2023;176:11c1–16.
5. Peres MF, Lerário DD, Garrido AB, Zukerman E. Primary headaches in obese patients. *Arq Neuropsiquiatr*. 2005;63:931–3.
6. Bigal ME, Liberman JN, Lipton RB. Obesity and migraine: a population study. *Neurology*. 2006;66:545–50.
7. Ávila BM, Zanini BM, Luduvico KP, Hense JD, Garcia DN, Prosczek J, Stefanello FM, Mason JB, Masternak MM, Schneider A. Effect of calorie restriction on redox status during chemically induced estropause in female mice. *Geroscience*. 2024;46:2139–51.
8. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care*. 2010;33:920–2.
9. Chen J, Li YT, Niu Z, He Z, Xie YJ, Hernandez J, Huang W, Wang HHX. Association of visceral obesity indices with Incident Diabetic Retinopathy in patients with diabetes: prospective cohort study. *JMIR Public Health Surveill*. 2024;10:e48120.
10. Chen D, Lu C, Chen K, Liu T, Li Y, Shan Z, Teng W. Association between anthropometric indices and hyperuricemia: a nationwide study in China. *Clin Rheumatol*. 2024;43:907–20.
11. Huang J, Han J, Rozi R, Fu B, Lu Z, Liu J, Ding Y. Association between lipid accumulation products and osteoarthritis among adults in the United States: a cross-sectional study, NHANES 2017–2020. *Prev Med*. 2024;180:107861.
12. Yu J, Yi Q, Chen G, Hou L, Liu Q, Xu Y, Qiu Y, Song P. The visceral adiposity index and risk of type 2 diabetes mellitus in China: a national cohort analysis. *Diabetes Metab Res Rev*. 2022;38:e3507.
13. Li Y, Zheng R, Li S, Cai R, Ni F, Zheng H, Hu R, Sun T. Association between four anthropometric indexes and metabolic syndrome in US adults. *Front Endocrinol (Lausanne)*. 2022;13:889785.
14. Liu Q, Huang Y, Wang M, Jiang H, Zhang X. Association of lipid accumulation products with testosterone deficiency in adult American men: a cross-sectional study. *Andrology*. 2023;11:551–60.
15. Kahn HS. The lipid accumulation product performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. *BMC Cardiovasc Disord*. 2005;5:26.
16. Peng H, Pan L, Ran S, Wang M, Huang S, Zhao M, Cao Z, Yao Z, Xu L, Yang Q, Lv W. Prediction of MAFLD and NAFLD using different screening indexes: a cross-sectional study in U.S. adults. *Front Endocrinol (Lausanne)*. 2023;14:1083032.
17. Johnson CL, Dohrmann SM, Burt VL, Mohadjer LK. National health and nutrition examination survey: sample design, 2011–2014. *Vital Health Stat 2* 2014;1–33.
18. Peng C, Gao L, Wu K, Jiang X, Chen X, Li C, Ge W, He L, Chen N. Association between the prognostic nutritional index and severe headache or migraine: a population-based study. *Nutr Neurosci*. 2023;26:1202–11.
19. Yan S, Chen S, Liu Y, Liang H, Zhang X, Zhang Q, Xiu J. Associations of serum carotenoids with visceral adiposity index and lipid accumulation product: a cross-sectional study based on NHANES 2001–2006. *Lipids Health Dis*. 2023;22:209.
20. Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. *Pain*. 2003;106:81–9.
21. Togha M, Haghdoost F, Khorsha F, Razeghi Jahromi S, Ghorbani Z. Body Mass Index and its Association with migraine characteristics in female patients. *Arch Iran Med*. 2019;22:554–9.
22. Gelaye B, Sacco S, Brown WJ, Nitche HL, Ornello R, Peterlin BL. Body composition status and the risk of migraine: a meta-analysis. *Neurology*. 2017;88:1795–804.
23. Ornello R, Ripa P, Pistoia F, Degan D, Tiseo C, Carolei A, Sacco S. Migraine and body mass index categories: a systematic review and meta-analysis of observational studies. *J Headache Pain*. 2015;16:27.
24. Kristoffersen ES, Børte S, Hagen K, Zwart JA, Winsvold BS. Migraine, obesity and body fat distribution - a population-based study. *J Headache Pain*. 2020;21:97.
25. Janoska M, Chorążka K, Domitrz I. Migraine frequency and its association with dyslipidemia in women. *Neurol Neurochir Pol*. 2015;49:95–8.
26. Tana C, Santilli F, Martelletti P, di Vincenzo A, Cipollone F, Davi G, Giamberardino MA. Correlation between migraine severity and cholesterol levels. *Pain Pract*. 2015;15:662–70.
27. Monastero R, Pipia C, Cefalù AB, Liveri ET, Rosano R, Camarda R, Camarda C. Association between plasma lipid levels and migraine in subjects aged > or = 50 years: preliminary data from the Zabùt Aging Project. *Neurol Sci*. 2008;29(Suppl 1):S179–181.

28. Qu K, Li MX, Yu P, Wu BH, Shi M, Dong M. HMG-CoA reductase is a potential therapeutic target for migraine: a mendelian randomization study. *Sci Rep*. 2024;14:12094.
29. Bruijn N, van Lohuizen R, Boron M, Fitzek M, Gabriele F, Giuliani G, Melgarejo L, Rehulka P, Sebastianelli G, Triller P, et al. Influence of metabolic state and body composition on the action of pharmacological treatment of migraine. *J Headache Pain*. 2024;25:20.
30. Guo Y, Daghlas I, Gormley P, Giulianini F, Ridker PM, Mora S, Kurth T, Rist PM, Chasman DI. Phenotypic and genotypic associations between Migraine and Lipoprotein Subfractions. *Neurology*. 2021;97:e2223–35.
31. Siewert KM, Klarin D, Damrauer SM, Chang KM, Tsao PS, Assimes TL, Davey Smith G, Voight BF. Cross-trait analyses with migraine reveal widespread pleiotropy and suggest a vascular component to migraine headache. *Int J Epidemiol*. 2020;49:1022–31.
32. Cancellor R, Clément K. Is obesity an inflammatory illness? Role of low-grade inflammation and macrophage infiltration in human white adipose tissue. *BJOG*. 2006;113:1141–7.
33. Schmidt FM, Weschenfelder J, Sander C, Minkwitz J, Thormann J, Chittka T, Mergl R, Kirkby KC, Faßhauer M, Stumvoll M, et al. Inflammatory cytokines in general and central obesity and modulating effects of physical activity. *PLoS ONE*. 2015;10:e0121971.
34. Cao H. Adipocytokines in obesity and metabolic disease. *J Endocrinol*. 2014;220:T47–59.
35. Peterlin BL, Sacco S, Bernecker C, Scher AI. Adipokines and migraine: a systematic review. *Headache*. 2016;56:622–44.
36. Bigal ME, Lipton RB, Holland PR, Goadsby PJ. Obesity, migraine, and chronic migraine: possible mechanisms of interaction. *Neurology*. 2007;68:1851–61.
37. Conti P, D'Ovidio C, Conti C, Gallenga CE, Lauritano D, Caraffa A, Kritas SK, Ronconi G. Progression in migraine: role of mast cells and pro-inflammatory and anti-inflammatory cytokines. *Eur J Pharmacol*. 2019;844:87–94.
38. Chai NC, Bond DS, Moghekar A, Scher AI, Peterlin BL. Obesity and headache: part II—potential mechanism and treatment considerations. *Headache*. 2014;54:459–71.
39. Domínguez C, Vieites-Prado A, Pérez-Mato M, Sobrino T, Rodríguez-Osorio X, López A, Campos F, Martínez F, Castillo J, Leira R. Role of adipocytokines in the pathophysiology of migraine: a cross-sectional study. *Cephalalgia*. 2018;38:904–11.
40. Peterlin BL. The role of the adipocytokines adiponectin and leptin in migraine. *J Am Osteopath Assoc*. 2009;109:314–7.
41. Perini F, D'Andrea G, Galloni E, Pignatelli F, Billo G, Alba S, Bussone G, Toso V. Plasma cytokine levels in migraineurs and controls. *Headache*. 2005;45:926–31.
42. Lassen LH, Haderslev PA, Jacobsen VB, Iversen HK, Sperling B, Olesen J. CGRP may play a causative role in migraine. *Cephalalgia*. 2002;22:54–61.
43. Zelissen PM, Koppeschaar HP, Lips CJ, Hackeng WH. Calcitonin gene-related peptide in human obesity. *Peptides*. 1991;12:861–3.
44. Recober A, Goadsby PJ. Calcitonin gene-related peptide: a molecular link between obesity and migraine? *Drug News Perspect*. 2010;23:112–7.
45. Ligong Z, Jinjin Q, Chunfu C, Congcong L, Xiaojun D. Effect of obesity and leptin level on migraineurs. *Med Sci Monit*. 2015;21:3270–4.
46. Sarchielli P, Rainero I, Coppola F, Rossi C, Mancini M, Pinessi L, Calabresi P. Involvement of corticotrophin-releasing factor and orexin-A in chronic migraine and medication-overuse headache: findings from cerebrospinal fluid. *Cephalalgia*. 2008;28:714–22.
47. Tsujino N, Sakurai T. Role of orexin in modulating arousal, feeding, and motivation. *Front Behav Neurosci*. 2013;7:28.
48. Milbank E, López M. Orexins/Hypocretins: key regulators of Energy Homeostasis. *Front Endocrinol (Lausanne)*. 2019;10:830.
49. de Mello AH, Costa AB, Engel JDG, Rezin GT. Mitochondrial dysfunction in obesity. *Life Sci*. 2018;192:26–32.
50. Chen J, Wang Q, Wang A, Lin Z. Structural and functional characterization of the gut microbiota in Elderly Women with Migraine. *Front Cell Infect Microbiol*. 2019;9:470.
51. Amabebe E, Robert FO, Agbalalah T, Orubu ESF. Microbial dysbiosis-induced obesity: role of gut microbiota in homeostasis of energy metabolism. *Br J Nutr*. 2020;123:1127–37.
52. Saad MJ, Santos A, Prada PO. Linking gut microbiota and inflammation to obesity and insulin resistance. *Physiol (Bethesda)*. 2016;31:283–93.
53. Farris SG, Thomas JG, Abrantes AM, Lipton RB, Burr EK, Godley FA, Roth JL, Pavlovic JM, Bond DS. Anxiety sensitivity and intentional avoidance of physical activity in women with probable migraine. *Cephalalgia*. 2019;39:1465–9.
54. Hamelsky SW, Lipton RB. Psychiatric comorbidity of migraine. *Headache*. 2006;46:1327–33.
55. Amiri S, Behnezhad S, Azad E. Migraine headache and depression in adults: a systematic review and Meta-analysis. *Neuropsychiatr*. 2019;33:131–40.
56. Lasserre AM, Glaus J, Vandeleur CL, Marques-Vidal P, Vaucher J, Bastardot F, Waeber G, Vollenweider P, Preisig M. Depression with atypical features and increase in obesity, body mass index, waist circumference, and fat mass: a prospective, population-based study. *JAMA Psychiatry*. 2014;71:880–8.
57. Jahromi SR, Martami F, Morad Soltani K, Togha M. Migraine and obesity: what is the real direction of their association? *Expert Rev Neurother*. 2023;23:75–84.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.