# Obesity, Migraine, and Overlapping Comorbidities in a Rural Pediatric Population

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## Abstract

**Objective**   This study aims to report the prevalence of obesity and overlapping comorbidities in a rural population of children and adolescents with migraine.

**Design and Methods**   A cross-sectional, descriptive, secondary data analysis using a comprehensive patient database from the West Virginia University (WVU) Medicine Epic Clarity system will be reported. A review of electronic medical records of 990 children and adolescents, ages 7 to 17 years, evaluated for headache at a rural clinic from December 1, 2009 to December 31, 2017 was completed. The Chi-square test was used to identify any differences in demographic characteristics (age, gender, and race) and distribution of comorbidities (obstructive sleep apnea syndrome [OSAS], depression, and anxiety) among obese versus nonobese adolescents with migraine. Student's $t$-test was used to identify any differences in the number of comorbidities between the two groups.

**Results**   A total of 648 children and adolescents with a diagnosis of migraine were identified. Approximately 26.4% of the children and adolescents diagnosed with migraine ($n = 648$) met the criteria for being obese with a mean body mass index (BMI) of 30.6 kg/m² (standard deviation [SD] = 6.5), ranging from 20.0 to 58.5 kg/m². There were no significant differences between migraineurs who were categorized as obese versus nonobese in terms of gender ($p = 0.8587$), age ($p = 0.1703$), race ($p = 0.7655$), anxiety ($p = 0.1841$), or depression ($p = 0.2793$). Obese individuals have more comorbidities than nonobese individuals ($p = 0.015$). Additionally, the prevalence of OSAS was significantly higher among obese versus nonobese migraineurs (20 vs. 9.9%, $p = 0.0007$).

**Conclusion**   Given the prevalence of obesity in rural pediatric populations and the reported neurobiological links between migraine and obesity, BMI needs to be monitored and weight management interventions included in plans of care for rural children and adolescents with migraine.

**Keywords**
► migraine
► rural
► obesity
► children
► adolescents
► comorbidities

## Introduction

Studies in children have shown that obesity is a risk factor in terms of migraine frequency and severity.[1] Rural children have a 26% greater odds of obesity, compared with urban children.[2] Also, lower socioeconomic status is associated with higher pain prevalence, especially for childhood and adolescent headache.[3] Comorbidities associated with childhood and adolescent obesity include sleep disorders, depression, as well as anxiety, and each of these overlap with migraine. Additionally, reported neurobiological links between migraine and regulation of body weight support the importance of monitoring body mass index (BMI) in rural pediatric patients with migraine.

The association between triggering of migraine and premonitory symptoms (i.e., food cravings, fatigue, and difficulty in sleeping) is based on the role of the hypothalamus in modulation of pain, control of appetite, and regulation of sleep.[4] Relationships between hypothalamic peptides (orexin), amino acid neuropeptides (CGRP), adipocytokines (adiponectin and leptin), and neurotransmitters (serotonin) with migraine and satiety (feeling of fullness and suppression of hunger) are examples of the neurobiological associations influencing obesity and migraine.[5]

Obesity is recognized as one of the most important risk factors for obstructive sleep apnea syndrome (OSAS) in the pediatric population. OSAS is observed in the obese population due to several mechanisms such as adenotonsillar hypertrophy, reduced lung volume associated with fat deposition around the abdomen and thorax, and increased airway collapsibility due to presence of fat at the level of the pharyngeal soft tissue.[6] Subsequently, pediatric migraine is a common comorbidity with OSAS due to disrupted sleep, hypercapnia, hypoxemia, elevation in systemic blood pressure, and elevated intracranial pressure.[7]

Adolescent headache is influenced by unhealthy lifestyle behaviors and depressed adolescents typically report unhealthier eating habits (processed foods, overeating, and binge eating), lower amounts of physical activity, higher sedentary behaviors, and greater screen time as compared with adolescents with no or lower depressive symptoms.[8] Anxiety has been reported as the most prevalent psychiatric comorbidity in children with tension-type headache and migraines.[9] Anxiety occurs more frequently in obese people when compared with those of normal weight.[10] A bidirectional relationship between obesity and anxiety, as well as depression and anxiety, has been reported.[8,11] Finally, undiagnosed depression and anxiety disorders increase the chronic nature of headaches, make headaches less responsive to treatment, and predict persistence of headache-related disability.

The above neurobiological links influencing obesity and migraine, as well as overlapping comorbidities, demonstrate the importance of monitoring BMI in rural children and adolescents presenting with headache. Migraine and obesity are considered public health problems which negatively impact quality of life.[12] Given the prevalence of obesity in rural children and adolescents, treatment of migraine alone may not only lead to poor headache outcomes but also a failure to address weight concerns and other comorbidities.

The purpose of this study is to (1) evaluate BMI in children and adolescents with migraine in a rural pediatric population, (2) evaluate the occurrence of comorbidities (OSAS, depression, and anxiety) in obese versus nonobese children and adolescents with migraine in a rural pediatric population, (3) determine if there is a significant difference in the presence of comorbidities between obese versus nonobese children and adolescents with migraine.

## Methods

### Design

This is a cross-sectional, descriptive, exploratory study using secondary data analysis.

### Setting and Sample

Approval for this study was obtained from the Institutional Review Board (IRB) as exempt. The sample was selected from a cohort of 990 children and adolescent ages 7 to 17 years who were evaluated for headache in a pediatric neurology clinic that is part of an academic medical center in rural North Central West Virginia between December 2009 and end of December 2017. The clinical population for this time-frame included only children and adolescents with a primary diagnosis of migraine ($n = 648$) based on classification standards.[13] Only those with migraine were included in this study for diagnostic clarity in evaluating migraine, obesity, and comorbidities.

### Measures

#### Demographic Characteristics

Gender, age, race, and ethnicity: demographic factors included participants' age (7–9 years, 10–12 years, and 13–17 years), sex (male and female), and race/ethnicity (non-Hispanic White, non-Hispanic African Americans, Hispanics, and others).

Obesity: age, height, weight, and sex were obtained from the electronic medical record (EMR). Based on the 2000 Centers for Disease Control and Prevention growth charts, obesity in youth was defined as a BMI of greater than or equal to the age- and sex-specific 95th percentile.[14] BMI was calculated using weight (lb)/(height [in ft])2 × 703. BMI percentiles were computed and included the following categories: (1) underweight (<5th percentile), (2) healthy weight (5th–<85th percentile), (3) overweight (85th–<95th percentile), and (4) obese (≥95th percentile).[14]

OSAS, depression, and anxiety: in this retrospective study of children and adolescents aged 7 to 17 years diagnosed with migraine,[13] charts were audited to identify the presence of the following diagnosis: OSAS, depression, and anxiety by International Classification of Disease, 10th or 9th Revision (ICD-10 or ICD-9) codes in the EMR.

### Data Collection

Data were obtained from the Integrated Data Repository (IDR), a comprehensive patient database that collects patient information from the West Virginia University (WVU) Medicine Epic Clarity system, housed at the West Virginia Clinical and

Translational Science Institute (WVCTSI). A data analyst from the WVCTSI retrieved EMR using structured query language (SQL) with the following inclusion criteria: pediatric patients aged 7 to 17 years evaluated in a rural pediatric neurology outpatient clinic within the span of December 1, 2009, to December 31, 2017, with at least one migraine diagnosis. All patients' records were deidentified from the extracted data.

### Statistical Analysis

The categorical variables were presented in their crude values along with the proportions and continuous variables were presented in the form of mean ± standard deviation [SD]. The main outcomes of interest include the occurrence of obesity in adolescents with migraine, as well as comorbidities associated with those who were obese or nonobese. The Chi-square test was used to identify the differences of demographic characteristics (age, gender, and race) and distribution of comorbidities (OSAS, depression, and anxiety) among obese and nonobese adolescents with migraine.

Specifically, Student's $t$-test was used to identify the difference of number of comorbidities between the two groups. Secondary analysis included the distribution of BMI categories among all adolescents with migraine, as well as stratified by gender. Outcomes of interest in the secondary analyses include count and percent of each weight category (underweight, healthy weight, overweight, or obese) and associated mean, SD, and range of BMI in each weight category. All statistical analysis was conducted using SAS (version 9.4; Cary, North Carolina, United States). The significance level was set at 0.05 and all $p$-values were two sided.

## Results

Demographics and comorbidities of obese and nonobese children and adolescents are presented in ►**Table 1**. Ethnicity comprised primarily white Caucasian (94.9%), followed by Black (1.5%) children and adolescents. Participants ranged in age from 7 to 17 years old, with the mean age being 12.6

**Table 1** Demographics and comorbidities of obese and nonobese children and adolescents with migraine

| Characteristics | All | Obese | Nonobese | p-Value |
|---|---|---|---|---|
| | (n = 648) | (n = 171) | (n = 477) | |
| Age (y) | | | | |
| 7–9 | 141 (21.8) | 29 (17.0) | 112 (23.5) | 0.1703 |
| 10–12 | 161 (24.9) | 48 (28.1) | 113 (23.7) | |
| 13–17 | 346 (53.4) | 94 (55.0) | 252 (52.8) | |
| Gender | | | | |
| Boy | 250 (38.6) | 65 (38.0) | 185 (38.8) | 0.8587 |
| Girl | 398 (61.4) | 106 (62.0) | 292 (61.2) | |
| Race | | | | |
| White | 615 (94.9) | 161 (94.2) | 454 (95.2) | 0.7655 |
| Black | 10 (1.5) | 2 (1.2) | 8 (1.7) | |
| Hispanic | 5 (0.8) | 2 (1.2) | 3 (0.6) | |
| Other | 18 (2.8) | 6 (3.5) | 12 (2.5) | |
| Comorbidities | | | | |
| OSAS | 81 (12.5) | 34 (20.0) | 47 (9.9) | 0.0007 |
| Depression | 133 (20.5) | 40 (23.4) | 93 (19.5) | 0.2793 |
| Anxiety | 183 (28.2) | 55 (32.2) | 128 (26.8) | 0.1841 |
| Only one comorbidity | | | | |
| OSAS | 47 (7.3) | 13 (7.6) | 34 (7.1) | |
| Depression | 43 (6.6) | 9 (5.3) | 34 (7.1) | |
| Anxiety | 78 (12.0) | 17 (9.9) | 61 (12.8) | |
| Two comorbidities | | | | |
| OSAS + depression | 4 (0.6) | 3 (1.8) | 1 (0.2) | |
| OSAS + anxiety | 19 (2.9) | 10 (5.9) | 9 (1.9) | |
| Anxiety + depression | 75 (11.6) | 20 (11.7) | 55 (11.5) | |
| Three comorbidities | | | | |
| OSAS + anxiety + depression | 11 (1.7) | 8 (4.7) | 3 (0.6) | |

Abbreviation: OSAS, obstructive sleep apnea syndrome.
Note: All percentages are calculated by columns.

(SD = 3.2) years. The sample was 61.4% female. Age was categorized by 7 to 9 years (21.8%), 10 to 12 year (24.9%), and 13 to 17 year (53.4%). There was no significant difference between the children and adolescents with migraine who were categorized as obese versus not obese in terms of gender ($p$ = 0.8587), age ($p$ = 0.1703), or race ($p$ = 0.7655). Approximately 26.4% ($n$ = 171) of the children and adolescents diagnosed with migraine ($n$ = 648) met the criteria for being obese. Comorbidities evaluated included OSAS, depression, and anxiety. OSAS was diagnosed in 12.5% ($n$ = 81) of the children and adolescents with migraine. Specifically, among the obese migraineurs, 20% ($n$ = 34) had obstructive sleep apnea, whereas among the nonobese migraineurs, only 9.9% had obstructive sleep apnea ($p$ = 0.0007). There was no significant difference in anxiety or depression between the children and adolescents with migraine who were classified as obese or nonobese.

Descriptive statistics of BMI and weight status between male and female are presented in ►**Table 2**. The prevalence of obesity among the children and adolescents with migraine was 26.4%, with mean BMI 30.6 kg/m$^2$ (SD = 6.5), ranging from 20.0 to 58.5 kg/m$^2$. One-fifth of these migraineurs were overweight, with mean BMI 23.1 kg/m$^2$ (SD = 3.1), ranging from 17.4 to 29.4 kg/m$^2$. The distribution of weight categories between male and female was not statistically significantly different.

When looking at the number of comorbidities, as shown in ►**Table 3**, there was a significant difference in the mean number of comorbidities between those migraineurs who

were classified as obese 0.75 (SD = 0.93) and those who were nonobese 0.56 (SD = 0.75; $p$ = 0.015). The analyses of number of comorbidities suggest that although the proportion of cases with at least one comorbidity is similar to those without comorbidity among obese and nonobese migraineurs ($p$ = 0.2136), the obese children and adolescents have a statistically and significantly higher percentage of at least two comorbidities (compared with those with one comorbidity) and three comorbidities (compared with those with two comorbidities) than nonobese individuals ($p$ = 0.0098 and 0.0112, respectively).

## Discussion

This is the first study to evaluate the association between obesity, migraine, and overlapping comorbidities in children and adolescents in rural West Virginia. The prevalence of adolescent obesity is 20.6% in the United States[15] and approximately 47% of children and adolescents in rural West Virginia are either overweight or obese.[16] In our sample ($n$ = 648), almost half of the children and adolescents with migraine were overweight or obese and, of these, 26% were obese (►**Table 2**).

There were no significant differences in children and adolescents with migraines who were classified as obese versus not obese in terms of gender, age, or race (►**Table 1**). In one of the largest studies examining weight diagnosis in a pediatric population, researchers found that increasing age was associated with an increasing prevalence of children with a BMI

**Table 2** Descriptive statistics of BMI and weight status between males and females with migraine

| BMI[a] | All | | Male | | Female | |
|---|---|---|---|---|---|---|
| | $n$ (%) | Mean (SD) [Range] | $n$ (%) | Mean (SD) [Range] | $n$ (%) | Mean (SD) [Range] |
| Underweight | 12 (1.9) | 15.0 (1.4) [13.2, 17.4] | 5 (2.0) | 15.4 (1.7) [13.4, 17.4] | 7 (1.8) | 14.6 (1.1) [13.2, 16.4] |
| Healthy weight | 330 (50.9) | 18.8 (2.7) [13.7, 25.1] | 130 (52.0) | 18.0 (2.4) [13.8, 24.0] | 200 (50.3) | 19.4 (2.8) [13.7, 25.1] |
| Overweight | 135 (20.8) | 23.1 (3.1) [17.4, 29.4] | 50 (20.0) | 21.7 (3.0) [17.4, 27.1] | 85 (21.4) | 23.9 (3.0) [17.7, 29.4] |
| Obese | 171 (26.4) | 30.6 (6.5) [20.0, 58.5] | 65 (26.0) | 28.4 (5.5) [20.0, 45.6] | 106 (26.3) | 31.9 (6.6) [20.6, 58.5] |

Abbreviations: BMI, body mass index; SD, standard deviation.
[a]Underweight = less than the 5th percentile; healthy weight = 5th percentile to less that the 85th percentile; overweight = 85th to less than the 95th percentile; and obese = equal to or greater than the 95th percentile.

**Table 3** Comparison in number of comorbidities between obese versus nonobese patients with migraine

| Number of comorbidities[a] | All ($n$ = 648) | Obese ($n$ = 171) | Nonobese ($n$ = 477) | $p$-Value |
|---|---|---|---|---|
| Mean (SD) | 0.61 (0.80) | 0.75 (0.93) | 0.56 (0.75) | 0.0150 |
| Zero comorbidity | 371 (57.3) | 91 (53.2) | 280 (58.7) | |
| One comorbidity | 168 (25.9) | 39 (22.8) | 129 (27.0) | |
| At least one comorbidity | 277 (42.7) | 80 (46.8) | 197 (41.3) | 0.2136[b] |
| Two comorbidities | 98 (15.1) | 33 (19.3) | 65 (13.6) | 0.0640[c] |
| At least two comorbidities | 109 (16.8) | 41 (24.0) | 68 (14.3) | 0.0098[d] |
| Three comorbidities | 11 (1.7) | 8 (4.7) | 3 (0.6) | 0.0112[e] |

Abbreviation: SD, standard deviation.
[a]Comorbidities: obstructive sleep apnea syndrome, depression, anxiety.
[b]Compares the number of cases with comorbidity absent versus comorbidity present between obese and nonobese patients.
[c]Compares the number of cases with one comorbidity versus two comorbidities between obese and nonobese patients.
[d]Compares the number of cases with only one comorbidity versus multiple comorbidities between obese and nonobese patients.
[e]Compares the number of cases with two comorbidities versus three comorbidities between obese and nonobese migraine patients.

≥85%.[17] However, these findings may be different from the current study due to the age range which included children 2 to 12 years of age as compared with age of this current study ranged between 7 and 17 years. For example, in a national U.S. data study, the prevalence of obesity among preschool-aged children (2–5 years; 13.9%) was lower than among school-aged children (6–11 years; 18.4%) and adolescents (12–19 years; 20.6%).[15] In the same study, researchers reported no statistically significant difference in the prevalence of obesity between male and female overall or by age group.[15] Also, there were no statistically significant differences in the prevalence of obesity between male and female by race and Hispanic origin.[15] Lack of reported findings with Hispanic and non-Hispanic black youth in the current study is associated with a lack of diversity in rural WV as evidenced by a racial/ethnic mix of 92% White, 4% Black, 0% Native American, 1% Asian, and 0% other with 1% Hispanic.[18]

OSAS occurs more frequently among children with obesity and is also a comorbidity with migraine. The prevalence of OSA has been reported at 44.6 to 56% in the obese pediatric population[19,20] and 40 to 56.6% in children with migraine.[21,22] The prevalence of this study was lower as 12.5% of the children and adolescents with migraine had OSAS and approximately 20% of those with OSAS were obese. These findings may be due to missed diagnoses of OSAS in this migraine population, as there is a general acknowledgment that the prevalence of OSAS is underestimated in children and adolescents.[23] Undiagnosed OSAS can lead to hypertension; cardiovascular disease; metabolic disorders; obesity; neuropsychiatric, developmental and behavioral issues; poor school performance; and daytime sleepiness.[23] Also, undiagnosed sleep disturbances are considered risk factors for more frequent and severe migraines, poorer headache prognosis, as well as headache chronification.[24]

There was no significant difference in anxiety or depression between the children and adolescents with migraine who were classified as obese or nonobese (►Table 1). However, approximately 40% of obese migraineurs and 34% of nonobese migraineurs were diagnosed with either depression or anxiety. Previous studies have reported a prevalence of at least one psychiatric disorder among pediatric patients with headache ranging from 29.6 to 65.5%.[9,25] These findings underscore the importance of monitoring for mental health issues when treating pediatric headache. Psychological consequences of childhood obesity include negative self-body image, weight-biased peer interactions, poor school experiences, and medical comorbidities which all interfere with the psychosocial development of a child.[26] Given the bidirectional relationships, undiagnosed or untreated psychiatric comorbidities contribute to both the onset and chronification of primary headaches.[11]

There was a significant difference in the mean number of comorbidities between those migraineurs who were classified as obese versus those who were nonobese (p = 0.015; ►Table 3). The mean number of comorbidities was higher in the children and adolescents with migraine that are obese versus those who are nonobese. Approximately 24% of the obese migraineurs had at least two comorbidities whereas only 14.3% of the nonobese migraineurs had at least two comorbidities. Thus, 24% of the children and adolescents

were diagnosed with obesity, migraine, and two (e.g., OSAS + depression, OSAS + anxiety, or anxiety + depression) or more comorbidities. Approximately 4.7% of the obese migraineurs had three comorbidities compared with 0.6% of the nonobese migraineurs. Therefore, 4.7% of the children and adolescents were diagnosed with obesity, migraine, depression, anxiety, and OSAS.

These findings demonstrate the importance of understanding the neurobiological links between migraine and obesity, as well as overlapping comorbidities. A thorough assessment to determine the presence of OSAS, depression, and anxiety can alert health care providers of the multifactorial contributors to migraine in the obese adolescent. Recognition and treatment of these overlapping comorbidities will optimize present, as well as future health outcomes in the pediatric migraine population.

## Strengths and Limitations

Strengths of this study include large sample size and a geographically distinct rural clinic. Diagnosis of migraine was determined by headache specialists using classification standards.[13]

BMI was calculated based on adolescent height and weight measured by clinic staff and recorded in the EMR as opposed to self-reported heights and weights which may not be as accurate. Limitations include use of a cross-sectional study design, where results are correlative; thus, causality cannot be addressed. The researchers relied on diagnosis codes to determine the occurrence of comorbidities and were not able to evaluate depression and anxiety using valid and reliable instruments nor do the researchers know if all the adolescents were appropriately evaluated for mental health or sleep disorders. There may be the potential for under- or overreporting of the comorbidities. A variety of medications may impact headache, weight, and mood and this review did not collect data on medications. Also, use of a clinic-based sample limits generalizability of our findings.

## Conclusion

The above findings underscore the importance of monitoring BMI in rural children and adolescents with migraine, as well as assessing overlapping comorbidities. Poor headache management during childhood leads to persistent headache into adulthood[27] and overweight children and adolescents are more likely to be overweight adults with poor physical and mental health.[28] When evaluating rural children and adolescents for primary headache, treatment can no longer be about migraine alone and must involve a holistic approach that includes evaluation of BMI. Given the association with migraine and overlapping comorbidities, obesity has been reported as a modifiable risk factor for migraine and weight loss as a feasible treatment option for improving headache outcomes.[29] Childhood and adolescent primary headache is influenced by unhealthy lifestyle behaviors[30,31] and addressing both mental health and obesity through a healthy lifestyle approach is also considered to be feasible and effective.[26] Treatment of obese pediatric migraineurs

should be targeted to therapies for restoring a healthy body-weight that includes exercise, diet, and behavioral interventions for weight loss. Further research is needed for evaluating weight management strategies that provide significant results in both migraine and BMI outcomes for obese rural adolescents.

### Note

### Funding

### Conflict of Interest

None declared.

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