RESEARCH ARTICLE



The effect of attention-deficit hyperactivity disorder symptoms on fracture occurrence in patients with osteopenia and osteoporosis

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ABSTRACT

Objective: Information and understanding of the relationship between attention-deficit hyperactivity disorder (ADHD) in adulthood and general medical conditions is limited. The aim of this study was to evaluate the relationship between ADHD symptoms and fractures in patients diagnosed with osteopenia/osteoporosis.

Method: A total of 100 patients (96 females, 4 males; aged 45-75 years) with a T-score of \leq 1 were included in the study. The ADHD symptoms of the participants were assessed using the Wender Utah Rating Scale (WURS) and the Adult ADHD Self-Report Scale (ASRS). The number of fractures, presence of systemic disease, and duration of treatment of the patients were recorded and analyzed.

Results: A significant difference in the total WURS and attention/irritability subscores was observed between the groups of those with and without a history of fracture. MANCOVA used to control confounding factors of gender, age, bone mineral densitometry values, presence of systemic disease and body mass index, revealed that the WURS irritability, attention, and total scores were significantly higher in the group with a history of fractures.

Conclusion: The results of this study of adults indicated that fracture occurrence was associated with attention and irritability symptoms of childhood ADHD. These findings may provide better insight and understanding of the lifelong, negative impact of ADHD on physical health.

Keywords: Attention-deficit hyperactivity disorder, fracture, osteopenia, osteoporosis

INTRODUCTION

Osteoporosis (OPS) and osteopenia (OPN), globally the most common metabolic bone diseases, are systemic skeletal diseases characterized by low bone mass and increased bone fragility and fracture risk due to microarchitectural deterioration of the bone tissue (1). OPS and OPN are conditions that have significant health consequences, particularly in the event of a bone fracture, and are becoming increasingly common, occurring in 60% to 70% of individuals over the age of 50 (2). OPS and OPN, in addition to other significant physical and psychological effects on patients, impose an important economic burden on the healthcare system (2). It is critical to take steps to reduce the physical, psychological, and economic impact of OPS, OPN, and other related fractures. The adult bone mass is based on the highest bone mass attained during adolescence and the plateau

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achieved in early adulthood before it begins to decline. In the normal, early cycle of bone remodeling and the cycle of build-destruction, the quantity of bone lost equals the amount of new bone formed. Imbalances in this modeling cycle that may occur for various reasons can result in OPN and OPS. OPS and OPN are usually diagnosed with a measurement of bone mineral density (BMD) in patients without a fragility fracture (3); however, dualenergy X-ray absorptiometry is the current gold-standard test used to diagnose OPS in patients without an osteoporotic fracture. A T-score of >-1 is considered normal, a score of -1 to -2.5 indicates OPN, and \leq -2.5 is classified as OPS. Although OPN and OPS can be present in any bone, the hips, spine, and wrists are the areas most likely to be affected. Hip fractures are the most personally and socially devastating in terms of death and cost (4). Fracture risk factors include advanced age, female gender, postmenopausal period, hypogonadism, low body weight, parental hip fracture history, smoking, alcohol consumption, vitamin D deficiency, and low calcium intake (5). Problems related to executive function, the cognitive skills necessary to control and regulate our daily behavior, have not been sufficiently investigated as a risk for fracture.

Attention-deficit hyperactivity disorder (ADHD) is one of the most common disorders related to executive function (6). ADHD is a neuropsychiatric disorder that begins in childhood, and is characterized by attention deficit, hyperactivity, and impulsivity. It has a prevalence of 5.29% in childhood (7), and 2.5% to 4.4% in adulthood (8). ADHD symptoms change with age; motor hyperactivity typically decreases in adulthood, and attention-deficit and impulsivity become the primary symptoms (8). ADHD symptoms can lead to serious adult problems, such as school/workplace difficulties and frequent job changes, poor organization, low self-esteem, inability to demonstrate skills, forgetfulness, and poor concentration (9). In addition to adverse effects on school/work performance, social life, and interpersonal relationships, ADHD also constitutes an increased risk for physical injuries and traffic accidents (10). This increased risk has been associated with impulsive and risk-taking behaviors and inattention (11,12). Barkley (12) suggested that as executive functions were impaired in individuals with ADHD, these individuals have more difficulty controlling and organizing behavior and emotions compared with the general population. These functions include cognitive processes, such as planning, problem-solving, and organizing goal-directed behavior. Therefore, ADHD symptoms may hinder the treatment of other accompanying medical problems and the

prevention of complications (13). There may be an increased risk of trauma/accident associated with neurodevelopmental disorders, such as developmental coordination disorder (14). Studies of children and adolescents with ADHD have reported a significant increase in traffic accidents and self-injury compared with their peers (15,16). Another study reported a non-fatal injury rate of 204 per 1000 in children/adolescents with ADHD compared with 115 cases per 1000 controls (adjusted odds ratio: 1.83) (17). Though ADHD is a well-established childhood disease, the data for adult patients are more limited.

A review of the current literature yielded few studies that have examined ADHD symptoms in patients with OPN and OPS. The present study was designed to investigate the association between traumatic and nontraumatic fractures and ADHD symptoms in patients with OPN/OPS. To our knowledge, this is the first study to explore this subject.

Hypotheses:

- 1. OPN and OPS patients with a fracture will have more attention-deficit symptoms than those without a fracture.
- 2. OPN and OPS patients with a fracture will demonstrate more symptoms of hyperactivity than those without fractures.
- 3. OPN and OPS patients with a fracture will show more signs of impulsivity than those without a fracture.
- 4. OPN and OPS patients with a fracture will exhibit more symptoms of irritability than those without fractures.

METHOD

The Selçuk University Ethics Committee approved this study. Written and verbal consent was obtained from the study participants.

Individuals aged 45-75 years were screened for inclusion in this cross-sectional study. A total of 173 consecutive individuals who presented at the Physical Therapy and Rehabilitation Outpatient Clinic of the hospital, and who had a BMD (femur total or lumbar vertebrae L1 to L4) value of \leq -1 were considered, and after application of the study criteria, 100 patients were enrolled. A history of any bone fracture at any time directed inclusion in the fracture group. A history of chronic systemic disease (hyperthyroidism, hyperparathyroidism, Cushing's disease, prolactinoma, hypogonadism, diabetes mellitus, malabsorption syndromes, liver disease, kidney disease, osteogenesis imperfecta, Marfan syndrome, homocystinuria, rheumatoid arthritis, ankylosing spondylitis, Nervosa, multiple myeloma), or systemic drug use (systemic glucocorticoids, levothyroxine, anticoagulants, antidepressants, lithium, antiepileptics, proton-pump inhibitors, antineoplastics, diuretics, aromatase inhibitors, gonadotropin-releasing hormone agonists) that could potentially affect the risk of fractures was cause for exclusion. In addition, those who were illiterate or diagnosed with intellectual disability, autism spectrum disorder, schizophrenia, bipolar disorder, or depression were not included in the research.

Two groups were formed: those with and without a history of fracture, and differences between the groups were evaluated. Sociodemographic data of age, gender, body mass index (BMI) measurement, occupation, education, and marital status were collected using a standard form, and the Wender Utah Rating Scale (WURS) and the Adult ADHD Self-Report Scale (ASRS) were administered to gather ADHD data.

Measures

Adult ADHD Self-Report Scale (ASRS): The ASRS was developed by the World Health Organization to screen adults for ADHD (18). A validity and reliability study of a Turkish version of the scale was conducted by Dogan et al. (19). The tool uses a 5-point Likert-type scale to assess each item. Attention deficit and hyperactivity/impulsivity subscales each consisting of 9 questions examine the patient's retrospective assessment of the frequency of symptoms over the previous 6 months. A score of \geq 24 in either subscale is classified as "highly likely ADHD," a score of 17-23 is scored as "likely ADHD," and a total of 0-16 is graded as "unlikely ADHD."

Wender Utah Rating Scale (WURS): The WURS is a 25-item scale that provides a quantitative evaluation of childhood ADHD symptoms to identify ADHD in adults. It is a 5-point Likert-type, self-report scale in which each item is graded 0-4 (0=not at all, 4=extremely) (20). The validity and reliability of a Turkish adaptation of the scale yielded a cut-off score of 36 (21).

Statistical Analysis

IBM SPSS Statistics for Windows, Version 23.0 software (IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis of the study data. An independentsample t-test was used to compare parametric continuous variables (such as age, scale scores) between groups. A chi-squared test was used to analyze categorical variables. Multivariate analysis of covariance (MANCOVA) was performed to reduce type II errors in multiple tests and assess confounding factors (age, gender, BMI, BMD, and presence of systemic disease). This analysis used the scores of all of the scales as outcome measures to determine primary effects. A p value of <0.1 was considered significant.

After the MANCOVA analysis, which revealed a significant difference between the fracture groups, a separate one-way analysis of covariance (ANCOVA) was performed using the outcome variables. Calculations of the effect size were made according to the percentage of variance yielded results of 0.01, 0.06, and 0.14 η^2 p, with 1%, 9%, and 25% as small, medium, and large effect sizes, respectively. Statistical significance was set at a p value of <0.05.

RESULTS

A total of 100 patients (female: 96, male: 4) between the ages of 47-75 were included in this study. The sociodemographic characteristics of the patients are presented in Table 1.

The participants were divided into 2 groups based on fracture history. An independent sample t-test was used to analyze the difference between the groups in the

Table 1: Sociodemographic characteristics of the study

| patients | | | |
|---------------------|----|--|--|
| n | % | | |
| Occupational status | | | |
| Working 79 | 79 | | |
| Not-working 21 | 21 | | |
| Educational level | | | |
| Illiterate 31 | 31 | | |
| Primary school 54 | 54 | | |
| High school 7 | 7 | | |
| University 8 | 8 | | |
| Systemic disease | | | |
| Yes 41 | 41 | | |
| No 59 | 59 | | |
| Treatment | | | |
| None 49 | 49 | | |
| <1 year 16 | 16 | | |
| 1-5 years 20 | 20 | | |
| >5 years 15 | 15 | | |
| Multiple fractures | | | |
| Yes 93 | 93 | | |
| No 7 | 7 | | |

WURS and ASRS scores, age, BMI, and BMD values, and a chi-squared test was used to analyze differences in terms of gender, occupation, educational status, and systemic disease. There was a significant difference between the groups in terms of attention, irritability, and the total WURS scores (Table 2).

The MANCOVA test results showed a significant difference between the groups in the whole sample (Pillai's trace V: 0.151, F (7, 86): 2.178, p<0.05,

 $\eta^2 p=0.151$). After the adjustment for scale scores, separate univariate ANCOVA was performed to compare 2 groups. The WURS-irritability scores (F[1.92]: 5.265, p=0.024, $\eta^2 p=0.054$), WURS-attention scores (F[1.92]: 7.743, p=0.007, $\eta^2 p=0.078$], and WURS-total scores (F[1, 92]: 4.265, p=0.042, $\eta^2 p=0.044$) were significantly higher in the group with a history of fracture than those of the non-fracture group (Table 3).

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| Table 2: Comparison of demographic and clinical characteristics | | | | |
|---|---------------|-------------|--------|------|
| | With fracture | No fracture | t/χ² | р |
| | n=34 | n=66 | | |
| Age (years) | 64.14±6.54 | 63.80±7.17 | -0.544 | 0.58 |
| Gender | | | | |
| Female | 33 (97%) | 63 (95%) | | |
| Male | 1 (3%) | 3 (5%) | 0.150 | 1.00 |
| Occupation | | | | |
| Working | 10 (29%) | 11 (17%) | | |
| Not working | 24 (71%) | 55 (83%) | 2.197 | 0.12 |
| Education level | | | | |
| Illiterate | 11 (32%) | 20 (30%) | | |
| Primary school | 16 (47%) | 38 (58%) | | |
| High school | 1 (3%) | 6 (9%) | | |
| University | 6 (18%) | 2 (3%) | 7.695 | 0.06 |
| Systemic disease | | | | |
| No | 11 (32%) | 30 (45%) | | |
| Yes | 23 (68%) | 36 (55%) | 1.592 | 0.28 |
| BMD-femur total | | | | |
| t | -1.35±0.95 | -1.04±0.77 | 1.717 | 0.09 |
| g/cm ³ | 0.81±0.11 | 0.85±0.10 | 1.752 | 0.08 |
| BMD-L1/L4 | | | | |
| t | -2.02±0.98 | -1.94±0.92 | 0.421 | 0.67 |
| g/cm ³ | 0.88±0.12 | 0.88±0.12 | -0.021 | 0.98 |
| ВМІ | 28.75±5.04 | 29.41±5.39 | 0.586 | 0.55 |
| WURS subscales | | | | |
| Irritability/conduct problems | 8.52±6.88 | 5.49±5.19 | -2.479 | 0.01 |
| Depression/mood difficulties | 5.26±4.54 | 4.74±4.11 | -0.581 | 0.56 |
| Impulsivity | 2.61±3.00 | 1.81±2.63 | -1.371 | 0.17 |
| Academic concerns | 3.44±2.64 | 2.90±2.72 | -0.935 | 0.35 |
| Inattention/anxiety | 7.05±3.95 | 5.07±3.07 | -2.768 | 0.01 |
| Total | 26.91±17.91 | 20.03±13.99 | -2.114 | 0.03 |
| ASRS | | | | |
| Attention deficit | 12.35±7.02 | 11.62±6.40 | -0.523 | 0.60 |
| Hyperactivity | 11.73±6.17 | 11.22±7.09 | -0.354 | 0.72 |
| Total | 24.08±12.10 | 22.84±11.73 | -0.495 | 0.62 |

ASRS: Adult Attention-Deficit Hyperactivity Disorder Self-Report Scale, BMI: Body mass index, BMD: Bone mineral density, WURS: Wender Utah Rating Scale

| | With fracture | No fracture | F | Р | η²p |
|-------------------------------|---------------|-------------|-------|-------|-------|
| WURS | | | | | |
| Irritability/conduct problems | 8.52±6.88 | 5.49±5.19 | 5.265 | 0.024 | 0.054 |
| Depression/mood difficulties | 5.26±4.54 | 4.74±4.11 | 0.392 | 0.533 | 0.004 |
| Impulsivity | 2.61±3.00 | 1.81±2.63 | 2.099 | 0.151 | 0.022 |
| Academic concerns | 3.44±2.64 | 2.90±2.72 | 0.724 | 0.397 | 0.008 |
| Inattention/anxiety | 7.05±3.95 | 5.07±3.07 | 7.743 | 0.007 | 0.078 |
| Total | 26.91±17.91 | 20.03±13.99 | 4.265 | 0.042 | 0.044 |
| ASRS | | | | | |
| Attention deficit | 12.35±7.02 | 11.62±6.40 | 0.087 | 0.769 | 0.001 |
| Hyperactivity | 11.73±6.17 | 11.22±7.09 | 0.264 | 0.609 | 0.003 |
| Total | 24.08±12.10 | 22.84±11.73 | 0.248 | 0.620 | 0.003 |

Table 3: Comparison of ADHD scale scores of groups (controlled for gender, age, BMD value, presence of systemic disease, and BMI)

ADHD: Attention-deficit hyperactivity disorder, ASRS: Adult Attention-Deficit Hyperactivity Disorder Self-Report Scale, BMD: Bone mineral density, BMI: Body mass index, WURS: Wender Utah Rating Scale, n²p: Partial eta squared

DISCUSSION

Although there have been some studies showing that fractures are more common in children/adolescents (22) and adults (23) with pre-existing ADHD, little is known about the relationship between fracture and ADHD symptoms in individuals diagnosed with OPN/ OPS. Our findings, which were controlled for the effects of BMD values, age, gender, and BMI, and demonstrate an association between WURS attention and irritability scores and fracture, are a new contribution to the literature. Although there is no clear causal relationship between ADHD symptoms and fracture formation, it may be that basic ADHD symptoms (attention deficit, hyperactivity, and impulsivity) and accompanying irritability may predispose an individual with OPN/OPS to fractures. Fractures/accidents have previously been associated with poor executive function, and deficiencies such as response inhibition and working memory, have been shown to contribute to the risk of fractures and accidents (24,25).

Thus far, there has been little published examination of the impact of ADHD symptoms on fractures in individuals diagnosed with OPN/OPS. It has been shown that risky behavior and accidents were significantly elevated in individuals with severe ADHD (26). It was observed in a study of participants aged 0-64 years that ADHD symptoms were associated with fractures, repetitive injuries, and the number of injuries (27). Chou et al. (28) found that ADHD signs and symptoms increased the fracture risk 1.32 times. Studies have also demonstrated that ADHD treatment reduced fracture risk among individuals aged \leq 40 years (29).

Our findings were consistent with our first hypothesis, and previous studies have shown that distraction was associated with a greater number of motor vehicle accidents and increased risk of fracture (30). Given that a fragility fracture was reported to be responsible for >80% of fractures in women >50 years of age and that these fractures were generally associated with minor traumas (31,32), attention would appear to be another important factor to be considered. It has been reported that the number of accidents and injuries may be 3 times greater as a result of attention deficit (25,33).

The literature also indicates that fractures and accidents have been associated with irritability and risktaking behavior (34), which was a hypothesis of this study that was confirmed by the data. Komurcu et al. (23) examined the impact of ADHD symptoms on fracture occurrence and noted that irritability, hyperactivity, and impulsivity symptoms may increase risk-taking. Also consistent with some of the findings in this study, all of the WURS subscores were significantly higher in the fracture group and extremity fractures were associated with ADHD symptoms in adults. In our group with a history of fracture, anger outbursts, which are not a basic symptom of ADHD, and irritability were significantly higher, potentially indicating behavioral problems. Anger is the defining emotional component of irritability, while aggression represents a behavioral component. Irritability in people with OPN/OPS may interfere with the behavioral control necessary for successful treatment and fracture prevention.

Our findings confirmed our first and fourth hypotheses; attention difficulty was related to clinically significant irritability and fracture. Earlier studies have noted that effective attention regulation is necessary for effective emotion regulation (35,36). Although our results did not support our second and third hypotheses, previous research has found a relationship between the severity of hyperactivity/impulsivity symptoms and fracture in children and adolescents (22). Predin et al. (37) reported that fractures were generally associated with the impulsivity/hyperactivity subscale. It may be that irritability in individuals with OPN/OPS and hyperactivity/impulsivity in children and adolescents have a noteworthy impact on fracture formation.

Limitations of this study include the fact that use of the WURS, though it is a standard ADHD measurement tool, must allow for recall problems, since it is administered retrospectively. In addition, the lack of psychiatric interviews and additional evaluation of ADHD and other psychiatric disorders (potentially confusing) may also be considered a limitation. Third, there were considerably fewer men than women in our study group. This will limit the generalization of data for male patients.

In conclusion, the results of this study demonstrated that there may be a significant link between fracture in OPN and OPS patients and the attention and irritability symptoms of ADHD. Prospective studies are needed to better explain and expand on our understanding of the relationship between fracture risk and ADHD symptoms.

| Contribution Categories | | Author Initials |
|-------------------------|-----------------------------------|-----------------|
| | Concept/Design | G.T. |
| Category 1 | Data acquisition | G.T. |
| | Data analysis/Interpretation | G.T. |
| Category 2 | Drafting manuscript | G.T. |
| | Critical revision of manuscript | G.T. |
| Category 3 | Final approval and accountability | G.T. |
| Other | Technical or material support | G.T. |
| | Supervision | N/A |

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Informed Consent: The parents of the participants provided written, informed consent before the study was initiated.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that there are no potential conflicts of interest.

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