Original Article

Atlantoaxial subluxation and Down syndrome: A cross-sectional analysis

ABSTRACT

Background: Atlantoaxial subluxation (AAS) is a diagnosis describing misalignment of the C1 vertebra relative to C2. Excessive translation of this joint, located adjacent to the medullary brain stem, can lead to devastating neurological consequences. A higher prevalence of AAS within the Down syndrome (DS) population has been well-established. This study aims to establish a prevalence rate of DS in patients hospitalized for AAS and compare outcomes between AAS patients with and without DS.

Methods: This study utilized the National Inpatient Sample (NIS) provided by the Healthcare Cost and Utilization Project (HCUP). In accordance with HCUP 2023 Clinical Classifications Software Refined files, data were queried using the International Classification of Diseases 10th Edition codes for DS and AAS. Demographics, comorbidities, hospital course, and outcomes were examined and compared using binary and linear multivariate regression. IBM SPSS software was used for data analysis.

Results: Of the 213,095 patients in the NIS database admitted between 2016 and 2020 with AAS as their primary diagnosis, 7.2% were DS patients. DS patients were significantly younger (26.56 ± 20.81 vs. 49.39 ± 27.63, $P < 0.01$), less likely to be female (33.30% vs. 52.10%), and had fewer comorbidities (diabetes mellitus, hypertension, and hyperlipidemia) than non-DS patients. There was no significant difference in likelihood to undergo surgical fusion between DS patients and non-DS patients with AAS.

Conclusion: This large-scale study using NIS data determined that 7.2% of all patients admitted to hospitals for AAS are DS patients. The analysis of demographics, hospital course, and outcomes can influence the development of treatment protocols for AAS in the DS population.

Keywords: Atlantoaxial, cervical, dislocation, Down syndrome, fusion, National Inpatient Sample, subluxation

INTRODUCTION

Atlantoaxial subluxation (AAS), dislocation, or instability are terms used to describe the misalignment of the C1 vertebra (the atlas) relative to C2 (the axis). This joint functions to support the occiput and protect the medulla of the brain stem while providing a range of motion to the cervical spine.[1] AAS has three main etiologies, with the first two being traumatic injury and chronic inflammatory changes secondary to conditions such as rheumatoid arthritis. The third major etiology of AAS includes congenital conditions, such as skeletal dysplasia, congenital osseous abnormalities, and Down syndrome (DS).[2]

While AAS is rare in the general population, the existing literature has established a clear association between

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AAS and DS.[1] This relationship is thought to be due to a combination of ligament laxity, degenerative bony changes, and low muscle tone. Although the condition is most commonly asymptomatic, 1%–2% of DS patients will experience symptoms due to spinal cord compression, including neck pain, gait disturbance, loss of sphincter control, upper motor neuron signs, or even paralysis and death. Thus, symptomatic AAS may constitute a medical emergency requiring urgent evaluation and possibly surgical intervention. The degenerative changes of AAS increase with age, and they occur earlier in DS patients than in the general population, further increasing the risk in these patients.[3]

There are competing prevalence rates cited among studies ranging from as low as 10%[4] to as high as 70%.[2] Studies exist with sample sizes in the hundreds, such as the 1984 study examining 236 DS patients and finding a 17% incidence rate.[5] However, a large-scale study has not been completed, nor have there been recent studies examining the prevalence at all. Recent studies of AAS in the DS population have been focused primarily on surgical intervention and outcomes of specific procedures.[6-8] Better defining the prevalence with modern data could lead to improved guide recognition, treatment, and future research in this area. Furthermore, there are currently no universally accepted guidelines for AAS treatment strategies in patients with DS versus those without, and the consistent output of literature surrounding the topic demonstrates the need for recognition and treatment of AAS in DS patients. Considering the increased prevalence of AAS in the DS population, data with potential to influence the development of treatment protocols will be useful for clinicians. In addition to re-examining the prevalence of DS in patients being treated for AAS, this study aims to analyze the outcomes of DS patients undergoing surgical treatment of AAS compared to patients without DS.

METHODS

Data source and patient selection

The National Inpatient Sample (NIS) database approximates a 20% stratified sample of all discharges from United States community hospitals, including over seven million encounters per calendar year. The NIS covers more than 97% of the U.S. population with a self-weighting design.[9] Access to such a large sample size allows researchers to establish incidence rates of relatively uncommon combinations of conditions, treatments, and initial outcomes based on documentation by clinical staff across the country. The NIS is the largest publicly available database provided by the Healthcare Cost and Utilization Project (HCUP) that includes inpatient admission data from participating institutions across the nation.

We queried the NIS from 2016 to 2020 for patients with a principal diagnosis of AAS using the International Classification of Diseases 10th Edition (ICD10) codes. ICD-10 codes were selected in accordance with HCUP 2023 Clinical Classifications Software Refined (CCSR) files. We then compared patients who had a concurrent diagnosis of DS (AAS-DS) to those who did not (AAS non-DS). The ICD-10 codes used to query the NIS database were as follows: DS-Q90.0, Q90.1, Q90.2, Q90.9; AAS-M43.11, M43.3, M43.4, M43.5 × 2, M43.8 × 1, M43.9, M53.2 × 1, S13.121A, S13.121D, S13.121S.

Data characteristics and outcome measures

Demographic variables such as age, sex, insurance status, and race were extracted. Comorbidities including diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLD), and obesity were examined. Hospital course, rates of surgery, and complications were also compared between AAS and AAS-DS patients. Primary outcomes measured were length of stay (LOS), whether patients were discharged directly home or into a skilled nursing facility, and inpatient death.

Statistical analysis

Descriptive analysis was performed to evaluate baseline characteristics. Pearson's Chi-squared test was used to compare categorical variables. Binary and linear multivariate regression was used in addition to odds ratio propensity score matching. All statistical analyses were conducted using SPSS Statistical Software (IBM Corp., released 2020. IBM SPSS Statistics for Windows, version 28.0. Armonk, NY, USA: IBM Corp.).

RESULTS

The NIS database documented a total of 213,095 DS patients admitted to hospitals between 2016 and 2020. Of these admissions, 495 (0.232%) had AAS as their primary diagnosis.

Demographics

Demographic analysis in Table 1 reveals that 7.2% of all patients admitted to hospitals for AAS have DS. AAS-DS patients were significantly younger than AAS non-DS patients (26.56 ± 20.81 vs. 49.39 ± 27.63, $P < 0.01$). AAS-DS patients were also less likely to be female (33.30% vs. 52.10%, $P < 0.01$), were more likely to have Medicaid insurance (32.30% vs. 19.50%, $P < 0.01$), and were more likely to be Caucasian (61.60% vs. 57.0%, $P = 0.02$) than AAS non-DS patients.

In comorbidity analysis, AAS-DS patients were less likely to have DM (4.00% vs. 12.30%, $P < 0.01$) and HTN (5.10% vs.

27.50%, $P < 0.01$) than AAS non-DS patients. AAS-DS patients were also less likely to have HLD (6.10% vs. 17.10%, $P < 0.01$) and obesity (3.00% vs. 5.30%, $P = 0.01$) than non-DS patients.

Hospital courses

Table 2 shows the hospital courses for patients admitted for AAS. There was no significant difference in likelihood to undergo cervical fusion between AAS-DS and AAS non-DS patients. In patients undergoing cervical fusion for AAS, there was no significant difference in rates of postoperative deep vein thrombosis or acute kidney injury. AAS-DS patients were more likely to develop pneumonia postoperatively (9.10% vs. 5.8%, $P < 0.01$) and less likely to develop urinary tract infection (4.00% vs. 9.00%, $P < 0.01$).

Outcomes

Table 3 shows outcomes following admission for all patients admitted for AAS. LOS was slightly shorter for AAS-DS patients than AAS non-DS patients (8.39 ± 8.84 vs. 9.04 ± 13.81, $P < 0.01$). AAS-DS patients were more likely to be discharged directly home (67.70% vs. 45.40%, $P < 0.01$) and less likely to be discharged into a skilled nursing facility (18.20% vs. 31.10%, $P < 0.01$). Inpatient death in the AAS-DS population was too small to report.

DISCUSSION

Although the association between AAS and DS is well-established, the prevalence of DS within AAS, as well as comparisons of outcomes between AAS patients with and without DS, has not been fully elucidated. This NIS study revealed that of the 213,095 patients in the NIS database admitted between 2016 and 2020 with AAS as their primary diagnosis, 7.2% were DS patients.

Considering the increased prevalence of DS patients among those presenting with AAS, it is crucial to evaluate and anticipate differences in treatment and recovery for this subset of the population. A notable finding our analysis demonstrated was that DS patients hospitalized for AAS were on average significantly younger when compared to the general population admitted for the same condition. The hypermobility secondary to collagen abnormalities associated with DS may be one factor that influences the earlier

Table 1: Demographics: Patients <65 admitted for principal diagnosis of atlantoaxial subluxation

Demographics	All (*n*=6920)	No DS (*n*=6425; 92.80%)	DS (*n*=495; 7.20%)	OR (95% CI)	*P*
Age	47.76±27.82	49.39±27.63	26.56±20.81		<0.01
Female	3515 (50.80)	3350 (52.10)	165 (33.30)	0.46 (0.38–0.56)	<0.01
Medicaid insurance	1410 (20.40)	1250 (19.50)	160 (32.30)	1.98 (1.62–2.41)	<0.01
Caucasian	3965 (57.30)	3660 (57.0)	305 (61.60)	1.21 (1.01–1.46)	0.02
Comorbidities					
Diabetes mellitus	810 (11.70)	790 (12.30)	20 (4.00)	0.30 (0.191–0.473)	<0.01
Hypertension	1795 (25.90)	1770 (27.50)	25 (5.10)	0.14 (0.09–0.21)	<0.01
Hyperlipidemia	1130 (16.30)	1100 (17.10)	30 (6.10)	0.312 (0.215–0.454)	<0.01
Obesity	355 (5.10)	340 (5.30)	15 (3.00)	0.559 (0.331–0.946)	0.01

DS - Down syndrome; CI - Confidence interval; OR - Odds ratio

Table 2: Hospital courses

	All (*n*=6920)	No DS (*n*=6425; 92.80%)	DS (*n*=495; 7.20%)	OR (95% CI)	*P*
Interventions					
Cervical fusion	1360 (19.70)	1275 (19.80)	85 (17.20)	0.837 (0.658–1.066)	0.08
Complications					
Deep venous thrombosis	180 (2.60)	170 (2.60)	10 (2.00)	0.759 (0.398–1.445)	0.25
Pneumonia	415 (6.00)	370 (5.80)	45 (9.10)	1.636 (1.184-2.262)	<0.01
Urinary tract infection	600 (8.70)	580 (9.00)	20 (4.00)	0.434 (0.269–0.669)	<0.01
Acute kidney injury	590 (8.50)	555 (8.60)	35 (7.10)	0.81 (0.565–1.147)	0.13

DS - Down syndrome; CI - Confidence interval; OR - Odds ratio

Table 3: Outcomes

	All (*n*=6920)	No DS (*n*=6425; 92.80%)	DS (*n*=495; 7.20%)	OR (95% CI)	*P*
LOS	8.99±13.52	9.04±13.81	8.39±8.84		<0.01
Discharge home	3250 (47.0)	2915 (45.40)	335 (67.70)	2.521 (2.075–3063)	<0.01
Skilled nursing facility	2090 (30.20)	2000 (31.10)	90 (18.20)	0.492 (0.389–0.622)	<0.01
Inpatient death	485 (7.00)	480 (7.50)	Too small to report	0.126 (0.052–0.306)	<0.01

DS - Down syndrome; CI - Confidence interval; OR - Odds ratio; LOS - Length of stay presentation of symptomatic AAS.[2] While degenerative vertebral translation takes years to develop, patients with congenital ligamentous laxity may be predisposed to an earlier presentation of symptoms. Another factor that may contribute to the younger presentation in DS is the increased likelihood of screening for AAS in patients diagnosed with DS. While recommendations for screening have gone in and out of favor over the last few decades, it is more likely that a DS patient will be screened for AAS when compared to a patient without DS, particularly when undergoing preparticipation evaluations for physical activity.[10-12] While recommendations supporting general screening for risk of future development of AAS in DS patients have been declining, it remains common for DS patients to be screened for asymptomatic AAS before engaging in new activities that may include forces to the head and neck such as gymnastics or contact sports.[13]

The younger age in the DS group may explain the lower rates of comorbidities when compared to the older, non-DS population admitted for AAS. DS patients were less likely to have diabetes, HTN, HLD, and obesity, which is likely to be a function of the 20+ year age difference between the cohorts.

As the atlantoaxial joint is located at the level of the medulla, translation may lead to compression, producing symptoms such as quadriparesis, apnea, hypotonia, and ataxia.[6] Although there is no consensus regarding exact parameters indicating surgical intervention, it is generally accepted that surgical intervention is warranted for neurological symptoms in the face of AAS. An additional parameter indicating surgical consideration in adults with AAS is having >5 mm of displacement between the posterior aspect of the anterior atlas and the anterior aspect of the odontoid process in adults (atlantodental interval).[14]

Since the prevalence of DS in the general population is approximately 8.27/10,000,[14] DS is clearly a predisposition for developing AAS given the 7.2% rate of DS in AAS patients in this study. Interestingly, our study revealed no significant difference in the probability of DS patients undergoing surgical fusion when compared to non-DS patients upon AAS admission. Of note, despite the comparable surgical likelihood between groups, surgeons often note difficulty performing fusion procedures in AAS-DS patients due to the increased hypermobility secondary to collagen defects in DS patients, making a stable fixation more difficult to achieve.[4] The statistically similar likelihood of proceeding with surgery despite the increased difficulty is encouraging evidence against discriminatory health-care choices made against patients with DS.

DS patients admitted for AAS were more likely to be discharged home and less likely to be discharged to a skilled nursing facility. Additional studies would be needed to ascertain the underlying cause of this finding; several possibilities include patients' baseline functional status, preadmission living situation (e.g., home vs. nursing facility), traumatic subluxation, and presence of spinal cord injury or myelopathy. The similar rates of surgery makes it unlikely that DS patients had less severe instances of subluxation leading to a higher likelihood of discharge home.

Regardless of the similarities in likelihood to undergo fusion, patients with DS were more likely to develop pneumonia as a postoperative complication which should prompt additional pulmonary precautions in the postoperative period. Elements such as patient support systems, insurance coverage, and location of skilled nursing facilities must all be taken into account before initiating a surgical plan.

Limitations

The authors recognize the limitations of this study, notably the retrospective nature of database analysis. The data rely on the accuracy of coding entry by thousands of clinicians across the country. To ensure accurate ICD-10 codes were selected, researchers used the 2023 HCUP CCSR files to fulfill the desired research queries. However, the NIS data do not include information regarding the severity of conditions, potentially introducing confounding factors when assessing outcomes.

CONCLUSION

In this large-scale, retrospective study using NIS data, we determined that 7.2% of all hospitalized patients admitted for AAS were DS patients. Consideration of demographics, hospital course, and outcomes, as examined in this study, can assist clinicians in the planning of surgical procedures and, critically, the planning of subsequent recovery and rehabilitation for AAS patients within the DS population.

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Conflicts of interest

There are no conflicts of interest.

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