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Cervical Instability in Down Syndrome: Beyond the Atlanto-Dens Interval. A Case- Control Study on the Role of Posterior C1 Arch Hypoplasia

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Abstract

Background

Cervical instability at the atlanto-axial and craniocervical junctions is a well- recognized phenomenon in children with Down syndrome (DS), with radiographic prevalences reported in the range of approximately 10% to 30%, yet the incidence of clinically manifest neurologic involvement remains low (around of 1–2%). Historically, routine radiographic screening of asymptomatic children with DS was widely adopted, particularly in the context of sports participation; however, more recent evidence and updated international guidelines have called into question the diagnostic accuracy and clinical utility of standard radiographic metrics.[3,4]

Objective

This retrospective case–control study aimed to evaluate the reliability of standard radiographic parameters in detecting cervical instability in children with DS and to assess the value of standard and dynamic radiographs. To this end, we used a control cohort of non-syndromic children presenting with atraumatic atlanto-axial subluxation (AAS).

Methods

Forty children with DS were compared with twenty-five non-syndromic children with traumatic AAS. Although the DS and AAS groups differed in clinical presentation and symptoms, the AAS group was chosen as a model of ligamentous-only instability with preserved bony anatomy. This pilot study was designed to derive insights into the osseous contribution to instability and, possibly, to identify useful cut-off values for cervical instability in non-syndromic pediatric patients. Three blinded observers measured standard radiographic indices, including the atlanto-dental interval (ADI), posterior atlanto-dental interval (PADI), space available for the cord at C1–C4 (SAC), Powers ratio, Harris BAI–BAI, X-line, Lee index, Chamberlain–McGregor lines, and C1 inclination angle. Interobserver reliability (ICC) and cross-index concordance (Fleiss' κ) were evaluated.

Results

Individual measurements showed good reproducibility (ICC > 0.70). Cross-index concordance was poor ($\kappa < 0.40$), meaning different indices frequently misclassify the same patient. PADI and SAC C1–C4 were significantly lower in DS patients ($p < 0.05$), consistent with posterior C1 arch hypoplasia and the synergistic effect of osseous anomalies and ligamentous laxity.

Conclusions

Plain static radiographic screening of asymptomatic children with DS has limited diagnostic accuracy and appears to play a limited role in clinical practice. On the other hand, dynamic radiographs and measurement of SAC at C1–C4, rather than ADI alone, combined with clinical assessment, may provide a more reliable evaluation of cervical instability.

1. Introduction

Cervical instability in Down syndrome (DS) represents a well-recognized clinical entity. Radiographic studies have consistently reported atlanto-axial or craniocervical instability in 10–30% of children with DS, whereas neurological symptoms develop in only approximately 1–2% of cases. [1,2] This discrepancy highlights a substantial gap between radiographic findings and clinical outcomes, driving decades of controversy over the indications and screening timeline.

The surgical literature offers an important perspective on the clinical relevance of this paradox. In published surgical series of DS patients requiring C1-C2 or occipito-cervical fusion, a vast majority presented with established myelopathy at the time of intervention, with proportions ranging from 75–89% in recent series. This finding carries a sobering implication: by the time surgery is indicated, irreversible cord damage may already be present. This suggests that traditional screening, which relies heavily on the ADI, is failing to identify the at-risk cord space, the period during which the canal is critically narrowed but the patient remains neurologically intact. The fact that all patients in these surgical series improved after stabilization (and that most presented with os odontoideum) points toward a chronic, structural rather than acute mechanism.

The ongoing debate regarding screening protocols reflects this clinical tension.The American Academy of Pediatrics (AAP) currently discourages routine radiographic screening in asymptomatic children with DS,[3,4] citing poor predictive value of standard radiographic parameters and the rarity of symptomatic progression. The 2025 World Federation of Neurosurgical Societies (WFNS) consensus, however, takes a more active position, advocating for dynamic flexion-extension radiographs from age five in high-risk syndromes such as DS and Morquio syndrome.[5]

In DS, cervical instability arises from the combined effects of ligamentous laxity and structural osseous dysplasia of the craniovertebral junction. Common anatomical abnormalities include posterior C1 arch hypoplasia, odontoid anomalies, and os odontoideum. Biomechanical studies have demonstrated that DS-specific bony morphology alone increases craniocervical motion by approximately 20–30% compared with age-matched controls, further supporting the contribution of skeletal anatomy to instability.[6] This finding arises the question of whether the simple ADI evaluation is enough or if the association of this parameter with other radiographic parameters can be more specific in detecting cervical instability.

The objective of this study was to evaluate the reliability and concordance of standard radiographic indices in a DS cohort and to operationally isolate the contribution of osseous dysplasia to cord space reduction by comparison with a non-syndromic group with ligamentous-only instability.

1.1 Study Hypothesis and Rationale for the Control Group

Given the complex interplay between ligamentous laxity and osseous dysplasia in Down syndrome (DS), a reference model of cervical instability with preserved bony anatomy is needed. Therefore, we selected children with traumatic atlanto-axial subluxation (AAS) as a control group. In non-syndromic children, AAS is typically an acute and often transient condition driven primarily by ligamentous insufficiency, while the underlying osseous anatomy remains preserved.

The use of AAS as a control group is not intended to equate these two conditions. Rather, AAS provides a model of ligamentous instability without the structural osseous abnormalities characteristic of DS, thereby allowing the osseous contribution to instability to be isolated and examined. Because AAS patients have intact bony anatomy, post-reduction measurements of the posterior atlanto-dental interval (PADI) and space available for the cord (SAC) at C1–C4 can serve as a reference for ligamentous-only instability. This approach enables the independent contribution of DS-specific osseous anatomical variations to spinal cord space reduction to be more directly quantified.

Furthermore, the identification of radiographic thresholds derived from this comparison may help establish clinically relevant cut-off values for C1–C2 instability, with potential diagnostic utility extending beyond the DS population to the broader pediatric population and other syndromic conditions associated with cervical instability, such as Morquio syndrome.

2. Materials and Methods

2.1 Study Hypothesis and Rationale for the Control Group

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beyond the DS population to the broader pediatric population and other syndromic conditions associated with cervical instability, such as Morquio syndrome.

2.2 Patient Selection and Study Design

This retrospective case-control study was conducted at Regina Margherita Children's Hospital (O.I.R.M.), Turin, between 2023 and 2025 (mean follow-up 20 months). The DS group included 40 (10,17 ± 2,52 y.o) children with trisomy 21 undergoing cervical instability screening as part of standard clinical follow-up, among them 1 presenting with os odontoideum and sings of instability and initial myelopathy underwent occipito-cervical fusion, representing 2.5% of our group population (in line with literature). The AAS control group comprised 25 non-syndromic children (7.87 ± 2.42 y.o), the majority with Grisel's syndrome, evaluated with dynamic radiographs approximately 45 days after the acute subluxation event, representing post-reduction condition. A part from the one underwent to surgery, no other patient in either group developed myelopathy or required surgical stabilization during follow-up.

2.3 Radiographic Measurements

Lateral cervical x-rays in standard, flexion, and extension were reviewed. Measured indices included: ADI (Atlanto-Dens Interval; instability threshold > 5 mm in children was considered), PADI (Posterior Atlanto-Dens Interval; threshold < 14 mm), SAC C1–C4 (Space Available for the Cord at each level), Power's ratio, Harris BDI and BAI, X-Lee line, Chamberlain and McGregor lines, and C1 inclination angle. Minimal acceptability required overlap of the acoustic meatus or mandibular angle on the lateral projection. Inadequate radiographs were excluded. All measurements were independently performed by three blinded observers, including one orthopedic surgeon and two radiologists (A.B., M.M., and L.B.).

2.4 Statistical Analysis

Inter-observer reliability was assessed by ICC (two-way mixed, absolute agreement). Cross-index concordance was assessed by Fleiss' kappa (κ): ≤0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, > 0.80 almost perfect.

3. Results

Seven patients in the DS cohort (17.5%) were excluded because of inadequate radiographic quality, particularly at the C0–C1 level (we assessed radiographic quality considering the head rotation and tilt if an overlap of auditory canal was present or not). No AAS controls were excluded.

3.1 Reliability (ICC)

Interobserver reliability was excellent, with ICC values exceeding 0.70 for all measured parameters in both groups.

3.2 Cross-Index Concordance (Fleiss' κ)

Cross-index concordance (Fleiss' κ) was uniformly below 0.40 across all parameter combinations. Patients classified as stable according to ADI were frequently classified as unstable according to PADI or SAC, and vice versa.

3.3 Radiographic Instability Prevalence

Between 15–25% of DS patients met radiographic instability criteria, depending on the parameter applied. Only one patient had neurological symptoms (initial myelopathy) during follow-up. Cervical migration of the dens was detected in 3 DS patients (0.75%), no case of cranial settling was found in control group

3.4 PADI and SAC C1–C4 Group Differences

PADI and SAC C1–C4 were significantly lower in DS patients than in AAS controls ($p < 0.05$). AAS controls showed preserved PADI and SAC at post-reduction evaluation, despite prior instability. DS patients, even those with normal ADI, showed reduced cord space due to posterior arch hypoplasia. This represents the "osseous penalty" of DS traducing in a increased risk for neurological involvement with the same ADI displacement.

4. Discussion

The principal finding of this study is that commonly used radiographic parameters for cervical instability in children with Down syndrome (DS) are not interchangeable. Although all measurements demonstrated good interobserver reliability (ICC > 0.70), agreement among indices was consistently poor (Fleiss' $\kappa < 0.40$). Consequently, the radiographic classification of instability depended substantially on the parameter selected. This finding is clinically relevant because current screening protocols continue to rely predominantly on the atlanto-dental interval (ADI), despite the possibility that other measurements identify a different subset of patients at risk.[3,4]

The poor concordance observed across radiographic parameters should not be interpreted as a methodological weakness but rather as evidence that these indices evaluate different components of cervical instability. ADI primarily reflects translational instability related to ligamentous insufficiency, whereas PADI and SAC quantify the residual space available for the spinal cord. As a result, a patient may present with a normal ADI while simultaneously demonstrating a critically reduced spinal canal reserve. This observation is consistent with previous studies reporting substantial variability in the radiographic assessment of the craniovertebral junction in children with DS[11] and poor correlation between ADI measurements and neurological outcomes.[12,18,19]

The comparison with the atraumatic atlanto-axial subluxation (AAS) cohort provides important insight into the pathophysiology of instability in DS. Unlike children with DS, AAS patients represent a model of predominantly ligamentous instability occurring in the setting of preserved osseous anatomy. Following reduction, these patients maintained normal PADI and SAC values despite a documented history of atlanto-axial instability. In contrast, DS patients demonstrated significantly reduced PADI and SAC values,

even in the absence of abnormal ADI measurements. This finding suggests that osseous abnormalities contribute independently to spinal canal narrowing.

The clinical relevance of this observation lies in the characteristic anatomy of the DS craniovertebral junction. Posterior C1 arch hypoplasia, odontoid abnormalities, and os odontoideum are common findings and may reduce the reserve space available for the spinal cord before substantial dynamic displacement occurs.[7,15] From a biomechanical perspective, ligamentous laxity and osseous dysplasia act synergistically. Whereas ligamentous insufficiency permits excessive motion, structural abnormalities reduce the capacity of the spinal canal to tolerate that motion safely. Consequently, children with DS may experience clinically significant cord compression despite degrees of atlantoaxial displacement that would be well tolerated in children with normal bony anatomy.

This concept is supported by the computational model proposed by Astin et al., which demonstrated that DS-specific craniovertebral morphology alone increases craniocervical motion by approximately 20–30% compared with non-DS controls with equivalent ligamentous properties.[6] Our findings provide a clinical correlate to these biomechanical observations. The significantly lower PADI and SAC values observed in DS patients, including those with normal ADI measurements, suggest the presence of an inherent structural reduction in spinal cord reserve. This “osseous penalty” may explain why neurological deterioration can occur despite apparently acceptable degrees of atlantoaxial displacement.

The clinical implications of these findings are reflected in the surgical literature. Recent series have reported that 75–89% of DS patients undergoing C1–C2 or occipitocervical fusion present with established myelopathy at the time of surgery.[8,9] While neurological improvement is commonly achieved after stabilization, many patients already demonstrate chronic spinal cord compromise and, in many cases, MRI evidence of cord injury.[8,9,16] These observations suggest that current screening strategies may identify instability relatively late in its natural history. The issue is therefore not whether surgery is effective, but rather whether instability is being recognized before neurological injury occurs.

The present findings suggest that, in DS, loss of spinal cord reserve may represent an earlier event in the natural history of instability, whereas measurable atlantoaxial displacement may occur later. This distinction may explain why patients can remain neurologically intact despite radiographic abnormalities and why many surgical patients present only after myelopathy has developed. It may also help explain the longstanding discrepancy between the relatively high prevalence of radiographic instability reported in DS and the much lower incidence of neurological symptoms.[18,19]

Particular attention should be given to patients with os odontoideum. In this setting, the odontoid fragment moves together with the anterior arch of C1, potentially resulting in relatively preserved ADI measurements despite marked reduction of the effective spinal canal diameter.[13] This represents a specific scenario in which ADI-based screening may underestimate the true severity of instability and further supports the inclusion of cord-space measurements in routine radiographic assessment.

A secondary contribution of this study is the use of the AAS cohort as a reference model for ligamentous-only instability. Because these children exhibited documented atlantoaxial instability in the absence of congenital osseous abnormalities, their post-reduction PADI and SAC values provide a practical reference for the expected spinal cord reserve associated with isolated ligamentous insufficiency. The significantly lower values observed in DS patients therefore offer an operational estimate of the independent osseous contribution to spinal canal narrowing. Future studies may use this reference model to define clinically meaningful radiographic thresholds applicable not only to DS but also to other pediatric conditions characterized by craniovertebral instability, such as Morquio syndrome.[17]

The findings of the present study may also have implications for future screening strategies. Current recommendations remain controversial because of the poor predictive value of traditional radiographic parameters and the low incidence of symptomatic progression.[3,4] However, the present results suggest that evaluation of spinal cord reserve through PADI and SAC measurements may provide clinically relevant information that is not captured by ADI alone. Future studies incorporating MRI may help determine whether reduced PADI and SAC values correlate with early spinal cord abnormalities and may contribute to the development of more clinically meaningful surveillance protocols.[16]

5. Limitations

Several limitations should be acknowledged. First, this study was retrospective, single-center, and based on a relatively small cohort, limiting the generalizability of the findings. Second, although the AAS cohort was selected as a model of ligamentous-only instability with preserved osseous anatomy, it should not be considered clinically equivalent to the DS population, given the different natural history and underlying pathophysiology of the two conditions. Another important limitation is the low incidence of neurological symptoms in our cohort. Only one patient developed early myelopathy during follow-up, preventing the identification of radiographic thresholds predictive of neurological deterioration. Consequently, the present study should be interpreted primarily as a pathophysiological investigation rather than as a threshold-defining study. The exclusion of 17.5% of DS radiographs because of inadequate image quality represents an additional limitation. Although this exclusion improved measurement reliability, it also reflects the practical difficulty of obtaining technically adequate cervical radiographs in children with DS and may limit the applicability of these findings to routine clinical practice. Finally, MRI data were not systematically available for all patients. While radiographic parameters provide indirect information regarding spinal cord reserve, MRI remains the reference standard for assessing spinal cord compression, signal changes, and dynamic neural compromise. Future studies incorporating dynamic MRI may further clarify the relationship between reduced PADI and SAC values and early spinal cord involvement.

Despite these limitations, the study provides a unique comparison between syndromic and non-syndromic cervical instability and offers preliminary evidence supporting an independent contribution of craniovertebral osseous abnormalities to spinal cord space reduction in children with DS.

Conclusions

Radiographic parameters commonly used to assess cervical instability in children with Down syndrome demonstrate good reproducibility but poor agreement, indicating that they evaluate different aspects of the disease process and should not be considered interchangeable. Compared with children with ligamentous-only atlantoaxial instability, DS patients showed significantly reduced spinal cord reserve, supporting an independent contribution of craniovertebral osseous abnormalities to instability. Dynamic radiographs combined with assessment of PADI and SAC may provide a more clinically meaningful evaluation than ADI alone and warrant further investigation in prospective studies incorporating MRI and long-term neurological follow-up.

Abbreviations

AAP
American Academy of Pediatrics
AAS
Atlanto-Axial Subluxation
ADI
Atlanto-Dens Interval
BAI
Basion-Axial Interval
BDI
Basion-Dens Interval
CT
Computed Tomography
CVJ
Craniovertebral Junction
DS
Down Syndrome
ENT
Ear, Nose and Throat
ICC
Intraclass Correlation Coefficient
JOA
Japanese Orthopaedic Association
MRI
Magnetic Resonance Imaging
O.I.R.M.
Ospedale Infantile Regina Margherita
PADI
Posterior Atlanto-Dens Interval

SAC
Space Available for the Cord
UNITO
Università degli Studi di Torino
WFNS
World Federation of Neurosurgical Societies
κ
Fleiss' kappa.

Declarations

AI Disclosure

During the preparation of this work the authors used Gemini and Claude (Anthropic) for English language assistance and to improve readability. The authors retain full responsibility for the scientific content, data accuracy, and clinical interpretations.

Author Contribution

Author Contributions:Conceptualization and article idea, Balagna, Spolaore, Aprato; data curation and formal analysis, Moretti, Balagna, Blasi; methodology, Balagna, Aprato, Rucci, Verna; writing—original draft preparation, Balagna, Rucci, Pezzi, Moretti; visualization, Verna, Rucci, Morello; writing—review and editing and/or critically revised the work, Balagna, Pezzi, Rucci, Spolaore, Verna, Morello, Blasi, Aprato. All authors have read and agreed to the final version of the manuscript.The manuscript and the related research have not been published and are not being considered for publication elsewhere, in whole or in part, in any language

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