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Brain and Spine 5 (2025) 104177

Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Prevalence and natural development of thoracolumbar kyphosis in achondroplasia: A systematic review and meta-analysis

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ARTICLE INFO

Handling Editor: Prof F Kandziora

Keywords:
Achondroplasia
Deformity
Dwarfism
Thoracolumbar kyphosis
Thoracolumbar spine

ABSTRACT

Introduction: Thoracolumbar kyphosis (TLK) is a frequently reported spinal deformity in achondroplasia, which in combination with the characteristic narrow spinal canal in achondroplasia predisposes for symptomatic spinal stenosis. There is however no consensus on the optimal treatment, due to limited data on diagnostic criteria, the natural development and the prevalence of TLK.
Research question: This study aims to assess the prevalence, natural development, and diagnostic criteria for pathological TLK in individuals with achondroplasia.
Material and methods: A systematic review and meta-analysis were conducted. Studies involving achondroplasia patients, which reported TLK measurement methods were included. The primary outcome was the pooled prevalence of TLK, stratified by age.
Results: Eight studies, encompassing 852 patients, met the inclusion criteria. Pathological TLK was most frequently defined as a Cobb angle of 20° or greater, between T10 and L2. TLK was present in 87% (95% CI 80%–91%) of patients under two years old, decreasing to 33% (24%–43%) at age three, 26% (19%–35%) between five and ten years, and 23% (16%–31%) in patients aged 10–20 years.
Discussion and conclusion: Pathological TLK in achondroplasia, defined as a Cobb angle of 20° or greater, appears primarily in early childhood and often resolves by walking age. However, approximately one-fourth of cases persist into adulthood, with factors such as developmental motor delay and vertebral wedging contributing to this persistence. Routine clinical and radiological evaluations during childhood, along with conservative management, are recommended to mitigate the need for surgery during adulthood.

1. Introduction

Achondroplasia is the most common type of skeletal dysplasia, with a reported prevalence of 4.6 per 100,000 live births (Foreman et al., 2020). This autosomal dominant condition arises from a genetic mutation affecting Fibroblast Growth Factor Receptor 3 (FGFR3), leading to aberrant proliferation and differentiation of chondrocytes (Li et al., 1997; Foldynova-Trantirkova et al., 2012). Common clinical features of achondroplasia include a small stature with rhizomelic shortening of the limbs, frontal bossing, a small chest, hypotonia, characteristic trident hands and spinal pathologies (Horton et al., 1978; Pauli, 2019). These spinal pathologies include lumbar hyper lordosis, a reduced interpedicular distance, and a thoracolumbar kyphosis (TLK) (Jeong et al., 2006; Pauli et al., 1997).

TLK is a non-congenital kyphotic deformity located on the thoracolumbar junction of the spine. In combination with narrowing of the spinal canal due to the short interpedicular distance, TLK predisposes for compression of the conus medullaris and/or cauda equina which can induce symptomatic spinal stenosis (Sciubba et al., 2007). This can lead to difficulties in walking, loss of motor strength in the legs, and neurogenic incontinence (Vleggeert-Lankamp et al., 2012). Additionally, the mere presence of this deformity can significantly impede daily comfort and functioning (Nahm et al., 2023).

The earliest development of TLK is often observed in infants during

Abbreviations: TLK, Thoracolumbar kyphosis; TLSO, thoracolumbosacral orthosis.

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https://doi.org/10.1016/j.bas.2024.104177
Received 19 September 2024; Received in revised form 15 December 2024; Accepted 30 December 2024
Available online 30 December 2024

the phase of independent sitting (Kopits, 1988). The combination of a disproportionately large head, generalized trunk hypotonia, and a small chest is likely to cause difficulty in maintaining an upright sitting posture, thereby predisposing the development of TLK (Pauli, 2019). Management depends on the severity of TLK and the presence of accompanying neurological symptoms, such as neurogenic claudication. Conservative management strategies include the prevention of unsupported sitting, combined with physical therapy, or the use of a modified thoracolumbosacral orthosis (TLSO) for bracing (Pauli et al., 1997). For more severe, progressive TLK, surgical intervention may be required. In the absence of neurological symptoms, deformity correction through posterior spinal fusion may be indicated. However, when neurological symptoms result from spinal cord compression associated with TLK, spinal fusion is typically combined with a decompressive laminectomy to alleviate the compression while simultaneously correcting the deformity (Ain et al., 2004a, 2004b; Margalit et al., 2018).

Although TLK is a continuous variable which describes the degree of kyphosis at the thoracolumbar junction, many studies dichotomize it into pathological and non-pathological TLK based on specific cut-off values. A systematic review conducted by our team in 2012 aimed to assess the prevalence of (pathological) TLK in achondroplasia, as well as the natural development. However, due to heterogeneity in the included study populations and no consensus on diagnostic criteria used to define pathological TLK, the review was unable to draw a definitive conclusion (Engberts et al., 2012). This lack of consensus renders it difficult to formulate diagnostic and therapeutic guidelines. While there has been an increase in research studying the development of TLK since the publication of this prior review, a comprehensive overview has not been made (Pauli, 2019). The objective of the current study was to perform a systematic review and meta-analysis on the literature regarding the prevalence, development, and diagnostic criteria of TLK in achondroplasia.

2. Material and methods

2.1. Literature search strategy

A systematic review and meta-analysis of the literature were performed by following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist (Page et al., 2021). A comprehensive search strategy in PubMed, Embase, and Web of Science was conducted to examine all English records that evaluated the prevalence and natural development of TLK in achondroplasia (Appendix A). Search terms included “achondroplasia” and “thoracolumbar kyphosis” with their relevant entry terms and variations. Dates of the search queries included articles from inception of each database up to and including June 2024.

2.2. Eligibility criteria

Selection of articles was independently performed by two reviewers (CO and CV-L). Articles were considered eligible for inclusion if the study population was exclusively comprised of individuals diagnosed with achondroplasia and if a clear indication of the prevalence of pathological TLK within the study population was provided, along with an age specification at the time of TLK assessment. Studies were excluded if there was no definition of pathological TLK provided, if there was no information on how TLK was measured, if TLK was not measured with an X-ray, or if the study population focused solely on patient cohorts subjected to brace treatment or surgical correction of TLK, as this does not reflect the natural development of TLK.

2.3. Risk of bias and quality assessment

Two investigators (CO and CV-L) independently performed a risk of bias analysis by assessing the included studies according to an adjusted Newcastle-Ottawa Scale (NOS) (Wells et al., 2013). Any discrepancies between the two investigators were resolved through consensus. The NOS has been adjusted to investigate the methodological quality of studies reporting the prevalence of TLK. Comparative studies that investigated the prevalence of TLK, but not as primary objective, had all data pooled into one group in this meta-analysis. Modifications were made to the NOS to suit cohort studies and case series reporting on prevalence data by adapting the selection criteria and removing the comparability criteria (Table B.1). Maximum scores were three for selection and three for outcome assessment, the comparability criterium was omitted as it was not relevant for assessing TLK prevalence. The quality of the study was then ranked as low ($\leq$2 points), moderate (3–4 points) or high (5–6 points) depending on the overall score. Studies only analyzing cohorts of specific age groups were considered representative of the overall study population, as the pooled results were stratified into different age groups in the meta-analysis. Due to the limited number of studies ($<$10) included in the analysis per age category, assessing the potential for small study effects through funnel plots was deemed unfeasible.

2.4. Data extraction and analysis

Data were extracted independently from each article by two investigators (CO and CV-L.). Disagreements between the reviewers were resolved by consensus. The following information was extracted from each study: author name, publication date, study design, sample size, demographic characteristics of participants, definition of pathological TLK, measurement method of TLK, prevalence of TLK stratified by age group, and the mean degrees of TLK between patients with- and without pathological TLK. Mean and standard deviation values of TLK reported in subgroups other than age (such as sex) were synthesized into a single group according to the guidelines in the Cochrane handbook to illustrate the natural development of TLK within an entire study population (Li et al., 2019).

A descriptive overview was made of the measurement method and definition used by each study to define pathological TLK. Subsequently, the primary outcome of interest was the pooled prevalence of TLK, stratified by age. Studies were included for qualitative analysis and not for pooled analysis if there were evident signs of selection bias, as reflected by the selection criteria in the NOS, if the age group categories were too broad for a subgroup analysis, or if there was an overlap in study cohorts between studies. Secondary outcomes were the natural development of TLK in patients with persistence of pathological TLK or withresolution of TLK. This was not meta-analyzed due to differences in age subgroups between studies and heterogeneity of the data.

Pooled data analysis utilized Comprehensive Meta-Analysis (CMA) version 4, employing the random-effects model according to the DerSimonian and Laird method to calculate the overall pooled prevalence for each age category, along with the respective 95% confidence intervals (CI) to assess both within and between-study variances (DerSimonian et al., 2007). Visual representation of estimates from individual studies and pooled point estimates was facilitated through forest plots. Heterogeneity among studies was assessed using the Cochrane Q test, with significance set at a p-value threshold $<$0.1. The I^2 index was employed to quantify the amount of variation attributed to between-study heterogeneity (Higgins et al., 2002).

3. Results

3.1. Literature search

The search strategy yielded a total of 520 results, with 163 articles from PubMed, 243 from Embase, and 114 from Web of Science (Fig. 1). After removal of duplicates and exclusion of articles that did not meet the inclusion criteria during the title and abstract screening process, 44 articles remained for full-text evaluation. Subsequently, eight studies

Table 1
Overview of the included studies.

Study, Year, Country	Study timing and design	Patient population	Sample size	Age at baseline	Follow-up duration	TLK definition[a]
Kopits, 1988, USA	Cross sectional	Achondroplasia patients of all ages	197	8.9 years (range 1 month – 76 years)	No follow-up	**Angle**: ≥15° **Vertebrae**: Apex between T12 – L2
Borkhuu, 2009, USA	Retrospective cohort	Children with radiographically and clinically confirmed achondroplasia	48	7 months (range 1–13)	5 years (range 2.3 – 10.7)	**Angle**: ≥20° **Vertebrae**: T11 – L2/L4[b]
Khan, 2016, USA	Retrospective case series	Achondroplasia patients without a history of spinal surgery	326	18 years	No follow-up	**Angle:** Mild TLK: 11° – 25° Moderate TLK: 26°–50° Severe TLK: >50° **Vertebrae**: T11 – L2
Margalit, 2018, USA	Retrospective cohort	Achondroplasia children under the age of 3 years with documentation of developmental milestones available	60	10.9 ± 7.0 months	5.7 ± 3.6 years	**Angle**: ≥20° **Vertebrae**: T12 – L1
Okenfuss, 2020, USA	Retrospective case series	Achondroplasia patients of all ages	89	5.1 years (IQR 0.62–17.5)	5.9 years	**Angle**: Not specified **Vertebrae**: T11 – L2
Ando, 2021, Japan	Prospective cohort	Children with radiographically and clinically confirmed achondroplasia	21	6 months (range 1–8 years)	7.7 years (range 5 – 16 years)	**Angle**: >20° **Vertebrae**: T10 – L2
Mok, 2022, South Korea	Retrospective cohort	Children with achondroplasia without a history of spinal surgery	49	16.6 ± 19.2 months	3.9 ± 2.0 years	**Angle**: ≥20° **Vertebrae**: T10 – L2
Da Silva, 2023, USA	Retrospective case series	Children with achondroplasia prior to walking age and with TLK >20° at baseline	62	10 ± 3 months	7 ± 4 years	**Angle**: >20° **Vertebrae**: Not specified

TLK – Thoracolumbar Kyphosis; USA – United States of America; IQR- Interquartile range.
[a] All Measurements were conducted in the sagittal direction on radiographs of the thoracolumbar spine, employing the Cobb angle methodology.
[b] The Cobb angle was measured at the vertebrae displaying the highest TLK value between T11 and either L2, L3, or L4.

were deemed eligible for inclusion in this systematic review (Kopits, 1988; Margalit et al., 2018; Khan et al., 2016; Borkhuu et al., 2009; Okenfuss et al., 2020; Ando et al., 2021; da Silva et al., 2023; Mok et al., 2022), of which seven were included in the meta-analysis (Kopits, 1988; Margalit et al., 2018; Khan et al., 2016; Borkhuu et al., 2009; Okenfuss et al., 2020; Ando et al., 2021; da Silva et al., 2023). Given the increase of research in this field, stringent inclusion criteria were applied to mitigate potential bias. Consequently, six of the seven studies included in the prior published systematic review (Engberts et al., 2012) were excluded due to one or more of the following reasons: Firstly, the study cohorts were solely comprised of patients who underwent surgery (Sciubba et al., 2007; Ain et al., 2006; Savini et al., 1991); secondly, there was either an inadequate description on the method of TLK measurements or a lack of a clear definition for pathological TLK (Bethem et al., 1981; Schkrohowsky et al., 2007; Kahanovitz et al., 1982), thirdly, there was insufficient information on the age distribution among the included patients (Sciubba et al., 2007; Savini et al., 1991; Schkrohowsky et al., 2007; Kahanovitz et al., 1982).

3.2. Description of studies

Characteristics of the eight included studies are provided in Table 1 (Kopits, 1988; Margalit et al., 2018; Khan et al., 2016; Borkhuu et al., 2009; Okenfuss et al., 2020; Ando et al., 2021; da Silva et al., 2023; Mok et al., 2022). Among the included studies, four were cohort studies, three were case series and one was a cross-sectional study. A total of 852 achondroplasia patients were included, with patients during early childhood, adolescence, and adulthood all being represented. Due to an overlap of patients between the cohorts of Margalit et al. (2018) and Khan et al. (2016), the true number of unique achondroplasia patients identified was 792. All eight studies investigated the prevalence of TLK in achondroplasia. Furthermore, four studies evaluated the natural development over time in the size of TLK in patients with persistent pathological TLK or with resolution of pathological TLK (Margalit et al., 2018; Borkhuu et al., 2009; Ando et al., 2021; Mok et al., 2022).

All studies evaluated TLK through the measurement of the Cobb angle at the thoracolumbar junction on a lateral radiograph. The predominant diagnostic criterium for pathological TLK was a Cobb angle threshold greater than- (or equal to) 20°. The upper thoracolumbar junction involved in the Cobb angle measurement varied from T10 to T12, while the lower thoracolumbar junction was most frequently measured at L2, with the exception for the approach employed by Margalit et al. (2018), where L1 was used. Khan et al. (2016) was the only study to identify subgroups in the severity of TLK: mild- (11–25°), moderate- (26–50°) and severe TLK (>50°). The prevalence for the subgroups of moderate- and severe TLK were synthesized into a single group during data extraction to increase comparability with the studies applying a 20-degree threshold, to enable pooled analysis with minimal heterogeneity. Margalit et al. (2018) and Da Silva et al. (2023)evaluated the prevalence of TLK in relation to developmental milestones (independent sitting age and walking age) instead of age, but also provided the mean age at which these milestones were attained.

3.3. Quality assessment

Based on the adapted Newcastle-Ottawa Scale (NOS), five out of the eight studies were rated as moderate quality, while three were rated as good quality(Table C.1). Points for representativeness of the cohort were not granted when patients that underwent surgery were excluded (Khan et al., 2016; Mok et al., 2022), if patients were only included if baseline TLK exceeded 20° (Da Silva et al., 2023), or if there was an inadequate description of the inclusion criteria (Okenfuss et al., 2020). The median

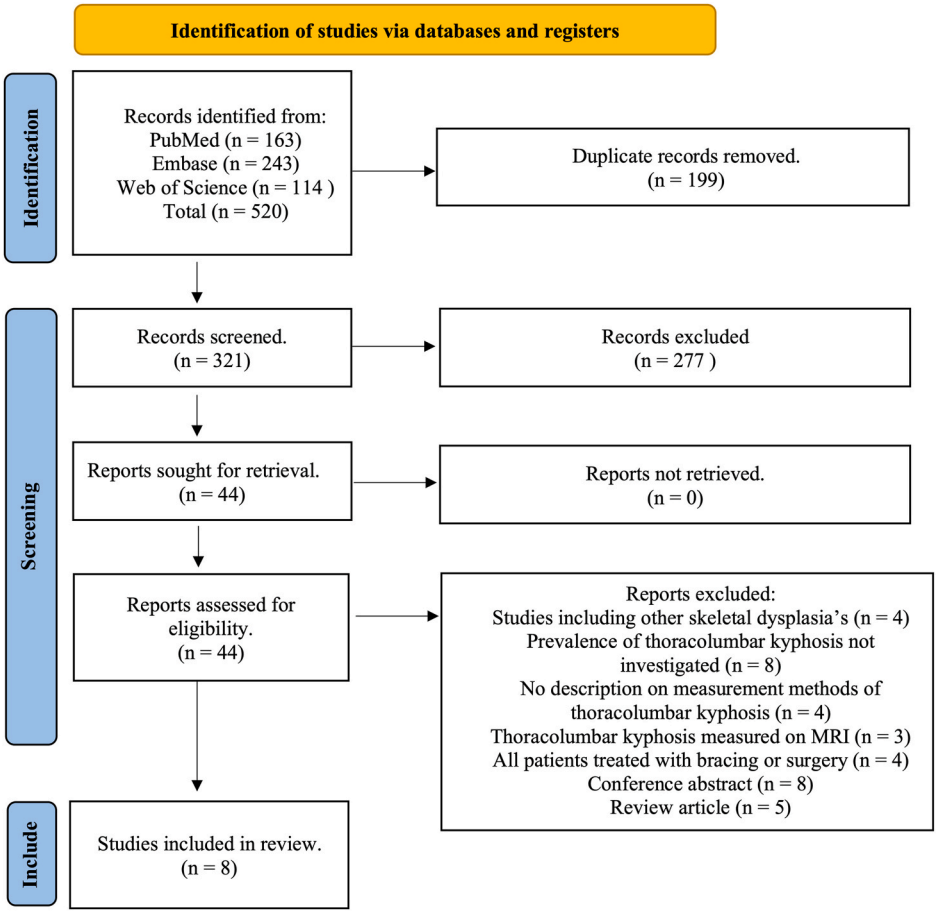

Fig. 1. Overview of study selection process.

overall score was 4, with scores ranging from 3 to 6.

3.4. Prevalence of TLK

Study specific details on the prevalence of TLK are provided in Table 2. Pooled analysis demonstrated that TLK was most prevalent during the initial two years after birth, affecting 87% (95% CI 80%–91%) of children with achondroplasia. The greatest change in TLK, without surgical intervention, occurred between ages 2 and 3 years, as the pooled prevalence decreased from 87% (95% CI 80%–91%) between the age of 0–2 years to 33% (95% CI 24%–43%) at 3 years. Margalit et al. (2018) and Borkhuu et al. (2009) described this age period as significant, as it corresponds to the period following attainment of independent ambulatory capability in children with achondroplasia (21.1 ± 7.8 months and 19.6 ± 6.6 months, respectively). In children aged 5–10 years, the prevalence of TLK decreased further to 26% (95% CI: 19%–35%) and it persisted during adolescence (10–20 years old) in 23% (95% CI 16%–31%) of patients (Fig. 2). Two studies demonstrated that the prevalence of TLK increased from adolescence into adulthood, although the adult cohorts largely consisted of patients with symptomatic spinal stenosis, thereby increasing the risk of selection bias and not being eligible for pooled analysis (Kopits, 1988; Khan et al., 2016).

Da Silva et al. (2023) was not included in the pooled subgroup analysis for children below the age of three because their inclusion criteria required children to have TLK greater than 20° at baseline, which would introduce selection bias. Khan et al. (2016) was excluded from analysis in the age category below two years due to an overlap of patients with Margalit et al. (2018). Mok et al. (2022) was not included in the pooled analysis because the TLK analysis was reported to be conducted after three years of age, but no further age details were provided, making it difficult to assign it to a specific age subgroup.

3.5. Natural development of TLK

Table 3 presents data concerning the natural development of TLK severity in patients, both those with persistent pathological TLK and those who have resolved their TLK (Margalit et al., 2018; Borkhuu et al., 2009; Ando et al., 2021; Mok et al., 2022). It is observed that despite patients falling below the threshold of 20°, TLK had not been completely resolved. However, all studies demonstrated that once TLK resolved below 20°, it is unlikely to recur. Ando et al. (2021) and Mok et al. (2022) illustrate that the mean disparity in the size of TLK between patients with resolved or persistent TLK increases with age. This is attributable to patients with persistent TLK experiencing a worsening of severity of kyphosis, while those without pathological TLK maintain a stable angle after resolution. These findings were not supported by Margalit et al. (2018), who demonstrated that the differences between both groups remained stable and never surpassed a 30-degree difference.

4. Discussion

This study was initiated following a systematic review published by our team in 2012 (Engberts et al., 2012), which concluded that the prevalence and natural development of TLK in achondroplasia could not be determined due to heterogeneity of study populations and the absence of consistent diagnostic criteria for pathological TLK. Our study reveals that the literature on this topic increased over the past decade, with the majority of studies included in this review adopting a sagittal Cobb angle of 20° at the thoracolumbar junction as a threshold. This

Table 2
Prevalence of thoracolumbar kyphosis, stratified by age, in each of the original studies.

Study, Year	TLK definition	TLK prevalence stratified by age
Kopits, 1988	**Angle**: ≥15° **Vertebrae**: Apex at T12-L2	<1 year: 94%; 1–2 years: 87% 2–5 years[a]: 39%; 5–10 years: 11% 10–15 years: 20%; 20–50 years[a]: 35%
Borkhuu, 2009	**Angle**: ≥20° **Vertebrae**: T11 – L2/L4	3 years: 35.4%
Khan, 2016	**Angle:** Mild TLK: 11°–25° Moderate TLK: 26°–50° Severe TLK: >50° **Vertebrae**: T11 – L2	0–2 years[a]: 88.33% TLK; 76.67% moderate- to severe TLK 3–12 years[a]: 83.76% TLK; 52.14% moderate- to severe TLK 13–19 years: 70.59% TLK; 35.29% moderate- to severe TLK 20–40 years[a]: 72.09% TLK; 41.86% moderate- to severe TLK 40 years[a]: 72.72% TLK; 49.09% moderate- to severe TLK
Margalit, 2018	**Angle**: ≥20° **Vertebrae**: T12 – L1	Baseline (10.9 ± 7.0 months): 89% At time of walking age (21.1 ± 7.8 months): 85% 1 year after walking age (33.1 ± 7.8 months): 42% After 5.7 year follow up: 30%
Okenfuss, 2020	**Angle**: Not specified **Vertebrae**: T11 – L2	At toddler age (≈3 years): 22%
Ando, 2021	**Angle**: >20° **Vertebrae**: T10 – L2	<1 year: 76.2%; 1 year: 85.7% 3 years: 33.3%; 5 years: 28.6% 7–10 years: 35.7%; 11–18 years: 33.3%
Mok, 2022	**Angle**: ≥20° **Vertebrae**: T10 – L2	>3 years[a]: 63.3%
Da Silva, 2023	**Angle**: >20° **Vertebrae**: Not specified	1 year after walking age (≈30 months)[a]: 35.5% 5 years: 25.8%; 10 years: 11.3%

TLK – Thoracolumbar Kyphosis; USA – United States of America.
[a] These age subgroups were not included in the pooled analysis for TLK prevalence.

Table 3
Natural development of thoracolumbar kyphosis (TLK) in patients with resolution or persistence of pathological TLK.

Study, Year	Age category	Angle in patients with resolution of pathological TLK (°)[a]	Angle in patients with persistence of pathological TLK (°)	Mean difference (95% CI)
Borkhuu, 2009	3 years	13.1 ± 5.5	37.2 ± 12.6	24.10 (17.81–30.39)
Margalit, 2018	Walking age (21.1 ± 7.8 months)	10.8 ± 6.0	39.9 ± 14.8	29.10 (23.46–34.74)
	1 year after walking (33.1 ± 7.8 months)	10.0 ± 4.4	33.7 ± 14.3	23.70 (17.92–29.48)
	After 5.7 year follow up	9.3 ± 4.5	37.7 ± 18.5	28.4 (19.75–37.05)
Ando, 2021	5 years	5.7 ± 3.7	38.2 ± 15.3	32.50 (21.00–44.00)
	7–10 years	6.0 ± 4.7	54.7 ± 17.9	48.70 (32.71–64.69)
	11–18 years	4.9 ± 2.6	68.4 ± 9.5	63.50 (50.10–76.90)
Mok, 2022	3 years 6 years 9 years 10 years	Not specified	Not specified	8.97[b] 28.05[b] 47.13[b] 52.93[b]

TLK – Thoracolumbar Kyphosis; CI – Confidence Interval.
[a] All Measurements were conducted in the sagittal direction on radiographs of the thoracolumbar spine, employing the Cobb angle methodology. Resolution of pathological TLK was defined as TLK below 20°.
[b] The mean difference was not provided, instead a Generalized Estimating Equation (GEE) coefficient was calculated that describes the effect of age as a covariate on the difference in the thoracolumbar angle between individuals with resolution- or persistence of TLK, as determined by a GEE analysis.

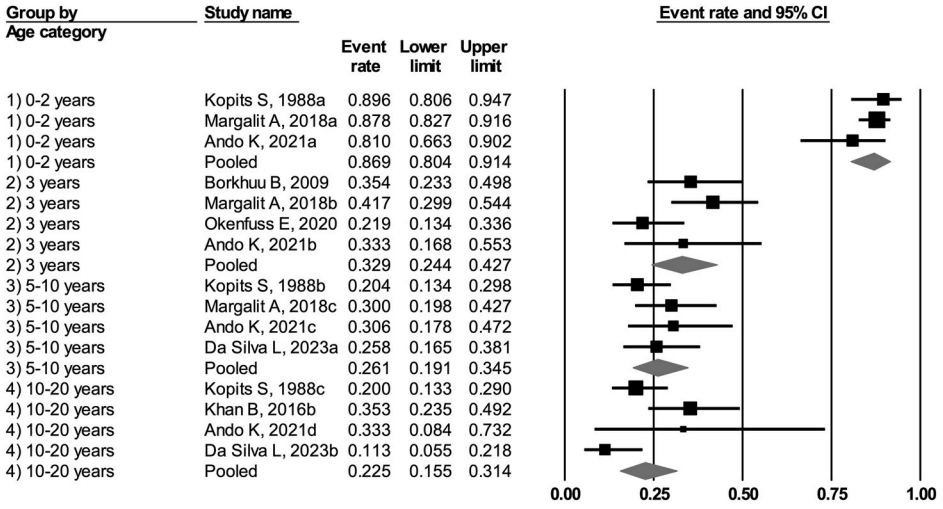

Fig. 2. Forest plot of pooled prevalence of TLK in achondroplasia stratified by age category
Prevalence of TLK in achondroplasia was categorized into separate age categories. A pooled prevalence (represented by the grey diamond) was calculated per age category by combining the individual prevalence (black squares) of the included studies for each age category. The 95% confidence intervals are reflected by the whiskers around the black squares for the individual point estimates and the width of the diamond for the different age categories.
TLK – Thoracolumbar Kyphosis; CI – Confidence Interval.

approach aligns with previous findings in individuals without achondroplasia by Bernhardt et al. (1989), who evaluated the range in Cobb angles at the upper thoracolumbar junction (T10 – T12) in a large group of patients without spinal pathology. It was demonstrated that the Cobb angle ranged from 3 degrees of lordosis to 20 degrees of kyphosis, thereby suggesting that a 20-degree Cobb angle can be applied as a cutoff point to identify pathological TLK. This may be disputed by stating that the thoracolumbar junction should be straight, and that any kyphotic alignment should be considered pathological. However, considering the high variability within a population, adopting such a strict criterion would result in overdiagnosis.

Based on results of this meta-analysis, TLK was most prevalent among infants under the age of two years, with a prevalence of 87%. Subsequently, there was a significant decline, with the prevalence decreasing to 33% by the age of three years. This rapid decrease in the development of TLK closely corresponds to the onset of independent ambulation, typically occurring around 24 months in children with achondroplasia (Ireland et al., 2012). This observed pattern supports the hypothesis that TLK in children is initially caused by difficulties in maintaining an upright seated posture. Factors such as macrocephaly, general trunk hypotonia and ligamentous laxity can lead to a C-sitting posture in response to gravitational forces (Pauli et al., 1997; Shirley et al., 2008). Long-term exposure to such forces can contribute to anterior vertebral wedging of the vertebrae over time, which in the literature is shown to be significantly associated with persistence of TLK and formation of a fixed deformity (Margalit et al., 2018; Borkhuu et al., 2009; Mok et al., 2022). In this meta-analysis, persistence of TLK occurred in approximately one fourth of patients with achondroplasia.

Developmental motor delay, along with vertebral wedging, is also identified in the literature as a risk factor for the persistence of TLK in achondroplasia, explaining the observed pattern of TLK's natural progression in this study (Margalit et al., 2018; Borkhuu et al., 2009). Delayed walking ability prolongs exposure to gravitational forces in an improper seated posture, thereby increasing the risk of fixed deformities forming due to vertebral wedging. Developmental motor delay may therefore be a predisposing factor for vertebral wedging. Vertebral wedging though, does not necessarily have to be a result of developmental motor delay. These findings highlight the importance of closely monitoring vertebral wedging and developmental milestones during early childhood to identify patients at risk for persistence of TLK. Monitoring should be particularly focused before the age of three, as the most significant changes tend to occur during this period and our results demonstrated that once TLK has been resolved, it is unlikely to recur.

During adulthood, TLK is significantly associated with the development of neurogenic claudication, gait disturbance, and urinary incontinence (Sciubba et al., 2007; Vleggeert-Lankamp et al., 2012; Schkrohowsky et al., 2007; Kahanovitz et al., 1982). Furthermore, progressive TLK can disrupt sagittal balance and cause compensatory lumbar hyper lordosis, which in achondroplasia is also linked to increased spinal stenosis (Cai et al., 2023, 2024). However, caution is necessary when interpreting TLK prevalence data in adults. Studies focusing on adult achondroplasia cohorts are more likely to contain patients with symptomatic spinal stenosis, which due to the correlation with TLK, will lead to an overestimate of prevalence of TLK in adulthood. Consequently, adult studies were not meta-analyzed in this review.

Treatment of TLK in adults with spinal stenosis may require posterior spinal fusion combined with a decompressive laminectomy, which carries substantial risk. Therefore, strict monitoring during childhood and an understanding regarding the natural development of TLK are crucial to prevent progression of TLK. Pauli et al. (1997) developed a conservative treatment protocol to prevent the need for surgery by avoiding unsupported sitting and utilizing bracing therapy. This guideline, which emphasizes early identification of TLK through clinical assessments every four to six months until age three and radiographs only upon suspicion of moderate or marked clinical kyphosis, has been widely adopted.

Despite publication of this guideline, this meta-analysis reveals that TLK still persists in 23% of patients. We therefore recommend incorporating routine radiological assessments alongside the clinical evaluations. Radiographs are more sensitive in identifying vertebral wedging, anomalies, and TLK than clinical examination alone. To minimize X-ray exposure, we suggest discontinuing radiographs when consecutive assessments show no signs of wedging or TLK progression, while continuing clinical examinations and prohibiting unsupported sitting. However, radiographs should be retaken at a low threshold if there is clinical suspicion of TLK progression. If wedging is observed, early brace treatment with a TLSO should be initiated, with regular radiologic reassessments every two to four months.

This systematic review and meta-analysis had several strengths, including a comprehensive literature search, a large collective patient cohort, especially considering the rarity of achondroplasia, and well-established inclusion criteria which led to a clear outline of the prevalence and natural development of TLK. Furthermore, stratification of the meta-analysis into subgroups allowed us to connect TLK findings to developmental milestones and delve into the etiology behind the persistence of TLK. There were also limitations: It was not possible to meta analyze the prevalence of TLK in adults, due to risks of selection bias. Finally, not all studies applied the same diagnostic criterium or measurement method for TLK, which introduces margins of heterogeneity. Future studies are advised to design a prospective follow-up study on the development of TLK from adolescence into adulthood. Additionally, further research will be conducted by our team to investigate risk factors related to progression of TLK in achondroplasia.

5. Conclusion

TLK is defined as a Cobb angle of 20° or more at the thoracolumbar junction. It is most prevalent under the age of two years, affecting 87% of children with achondroplasia. This prevalence spontaneously declines to 33% by age three, after which the natural development slows down. TLK persists into adolescence and adulthood in 23% of patients, with developmental motor delay and vertebral wedging likely contributing to this persistence. Routine clinical and radiological examinations during childhood alongside conservative treatment are recommended to prevent the need for surgery during adulthood. Further research into risk factors for development of persistent TLK are warranted to provide more insight into the optimal treatment of TLK.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Each author acknowledges with gratitude the work of Jan W. Schoones, Directorate of Research Policy, for his assistance in developing the literature search strategy in this systematic review.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bas.2024.104177.

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