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REVIEW ARTICLE

Current biomechanical theories on the etiopathogenesis of idiopathic scoliosis

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Abstract

Purpose There is great controversy about the etiologic origin of adolescent idiopathic scoliosis. Multiple theories have been suggested, including metabolic aspects, endocrine dysfunction, neurological central abnormalities, genetic predisposition and epigenetic factors involved in the development of scoliosis. However, there has always been speculations based on human biomechanical behavior.

Methods In this article, we performed a literature review on the biomechanical traits of human posture, and the proposed theories that explain the special characteristics present in idiopathic scoliosis.

Results The current theory on the etiopathogeneis of AIS suggests that dorsally directed shear loads acting on a preexisting axial plane rotation, in a posteriorly inclined sagittal plane of a growing patient, together with disc maturation, collagen quality at this phase of development and immaturity of proprioception, is the perfect scenario to spark rotational instability and create the three-dimensional deformity that defines idiopathic scoliosis.

Conclusion The unique spinal alignment of human bipedalism, gravity and muscle forces acting straight above the pelvis to preserve an upright balance, and the instability of the soft tissue in a period of growth development, is an appealing cocktail to try to explain the genesis of this condition in humans.

Keywords Idiopathic scoliosis · Etiopathogenesis · Spine biomechanics · Spinal shear loads · Vertebrae rotation · Disc maturity

Introduction

Although a lot of research has been done in the field [1], there is still no current agreed theory demonstrating the exact etiopathogenesis of adolescent idiopathic scoliosis (AIS). The term idiopathic cannot be erased, as this condition has yet to be proven to be linked to a pathological state. One of the main difficulties we encounter in this endeavor is that we are searching for answers analyzing an already established deformity. We have not been able yet to create an experimental model that truly resembles human scoliosis. One of the lines of thought imputes gravity acting in bipedalism as a potential driver for scoliosis. Thus, some authors have tried to convert quadrupeds into bipeds, mostly in chicken, rabbits and rats [2]. However, all required drastic surgical or systemic interventions, and they are far from representing the status of human bipedalism. Nevertheless, other non-bipedal species (fish for example) are also known to develop scoliosis (water stream resistance could the driving force in these cases) [3]. Thus, we do not have an insight on scoliosis origin at its early stages, it is impossible to understand its cause if we only have access to the end product, which is the resulting deformity.

Review of the proposed etiologies of AIS

Melatonin deficiency after pineal gland resections in chickens led to scoliosis development, and some authors have detected decreased serum levels of melatonin in patients

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with progressive deformities [4]. It seems that the absence of this hormone could interfere with skeletal growth and symmetrical development of their proprioceptive system [5]. On the other hand, some authors have failed to confirm this theory in primates (rhesus monkeys) [6] or unbalance on serum levels in AIS patients. So experiments in lower animal models are different from primates, and findings in lower animals cannot necessarily be extrapolated to human beings [7].

Other metabolic dysregulations could interfere with growth. Higher levels of Growth Hormone (GH) and somatomedin have been found in AIS patients, but this is based on small trials that are neither conclusive nor updated [8]. Calmodulin regulates contractile properties of muscles interacting with myosin and actin. Asymmetric distributions of calmodulin have been detected in the paraspinal muscles of AIS patients, and an increased concentration of calmodulin in the platelets of AIS was associated with curve progression [9, 10]. Low leptin levels have been spotted in these patients, and this protein contributes to body weight, body mass index and bone mineral density, eventually interacting with body growth. In fact, selective hypothalamic dysfunction with upregulation sensitivity to circulating leptin creates skeletal asymmetries [11, 12].

Abnormal bone mineralization in combination with increased bone growth during the growth spurt can disturb bone microarchitecture, affect mechanical bone strength, and contribute to the vicious circle of the deformity [13, 14]. Therefore, osteoporosis and lower levels of serum vitamin D have been associated with the development and progression of AIS [15].

All these metabolic hypotheses have been extensively reviewed, and the predictive values of all these parameters for curve progression are still limited and based in low levels of evidence [16].

The vestibulo-ocular-spinal axis is related to balance and proprioception, so central disorders may be incriminated in the development of AIS. Visuo-oculomotor dysfunction [17], hidden neurologic impairment [18], brain interhemispheric asymmetry function [19]; all of them can contribute to asymmetric muscle activation of the paraspinal muscles and are proposed as neuromuscular subclinical etiology of AIS. There are findings supporting the hypothesis that a sensorimotor integration disorder underlies the pathogenesis of idiopathic scoliosis [20]. Surface electromyographic analysis detected visible disturbances and asymmetries in the erector spinae frequency (activity and tension) correlating with curve side [21] and the convexity of the curve [22].

A review was conducted to assess how strong the current evidence is in favor of all the different anomalies associated with idiopathic scoliosis [23] and an overall weak evidence was found for any consistent pattern of co-occurrence of AIS and any abnormality.

Familial clustering and studies in twins have shown a genetic predisposition for scoliosis [24], multiple genes have been associated with idiopathic scoliosis [25, 26], the most important have been recently summarized in a review article [27]. However, the exact mode of inheritance is not yet established, partially due to the genetic heterogeneity of scoliosis [28]. The ScoliScore project was launched in 2010 as the first genetic DNA-based test for predicting AIS progression using an algorithm incorporating results from 53 single nucleotide variants (SNVs) and the Cobb angle of Caucasian US teens [29]. Unfortunately, several separate independent research teams were unable to reproduce these findings in subsequent Japanese [30], French Canadian [31] or Han Chinese populations [32], and the use of the test was progressively abandoned.

The development of efficient gene editing methods and high throughput sequencing technology is promising for future research. Zebrafish are increasingly being used as a model thanks to their high genetic homology with humans [3].

Recently epigenetics and specific biomarkers are been studied to clarify the etiology and potential progression of idiopathic scoliosis [33]. There is a hypothesis that supports epigenetic internal and external environmental factors that affect vertebral growth during childhood in a pre-existing heritable genetic variation [34].

Apart from the above-mentioned theories, biomechanical hypotheses have always been debated. In this paper, we will focus on the current biomechanical approach to scoliosis.

The biomechanical approach to scoliosis

Scoliosis is a 3D deformity of the human trunk. Classical anatomists like Adams 1864, Meyer 1866, or Nicoladoni 1904 were already aware of the 3D nature of scoliosis, and were able to describe the anatomical changes of discs and vertebrae in scoliotic specimens. These anatomic abnormalities have been further studied with modern technology (EOS low-dose radiograph system, magnetic resonance imaging, and computed tomography scan) [35–38] (Fig. 1). However, idiopathic scoliosis does not occur naturally in other mammals apart from humans [2], and strong forces need to be applied in experimental studies in order to biomechanically force spines to curve. The unique spinal alignment of human bipedalism, gravity and muscle forces acting to preserve an upright balance, and the instability of the soft tissue in a period of growth development, is an appealing cocktail to try to explain the genesis of this condition in humans.

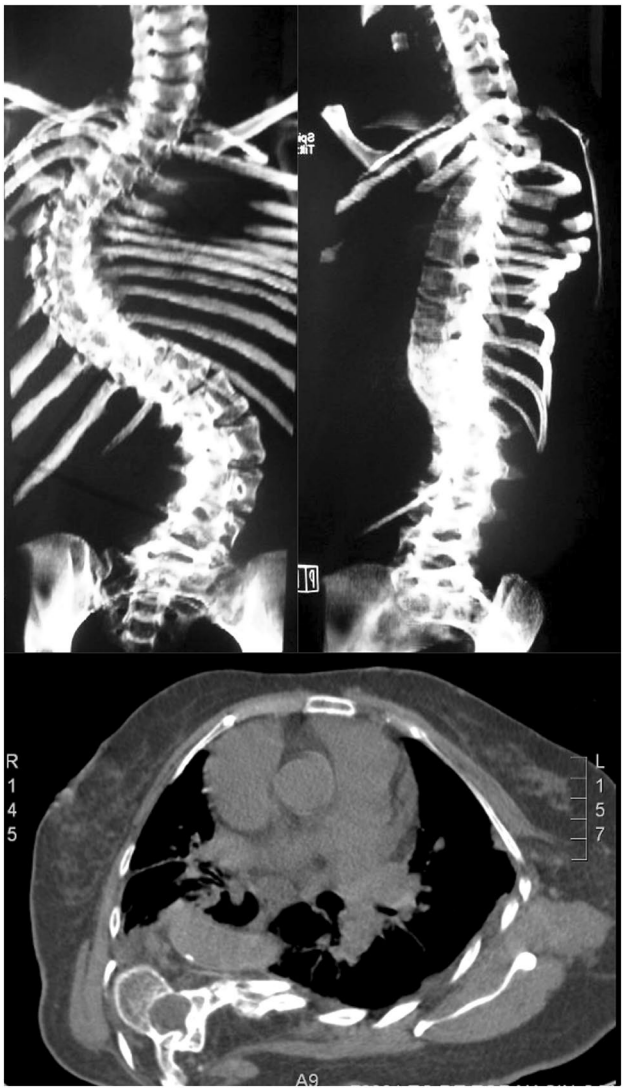

Fig. 1 3D deformity of scoliosis shown in a CT scan, affecting the coronal, sagittal and axial plane of the spine

Biomechanics of the upright human spine

Humans are unique in their spinal alignment. Apes became bipedal in great amount thanks to changes occurring in the pelvis. The pelvis became wider (pelvic incidence increased), more horizontal, and lordotic within the ischio-iliac angle relationship [39]. These facts led to the development of lumbar lordosis (to accommodate to the upright position) and to a change in the orientation of the hips allowing hip and knee extension (that enabled humans to walk efficiently with the minimal use of energy) [40, 41]. With this structure, the center of gravity lies straight above the pelvis instead of in front of the pelvis compared to other vertebrates, changing completely spinal biomechanics (Fig. 2).

All deformities of the skeleton are originated by a disturbance of the relation between the forces applied and the counteracting structures. In quadrupeds, the main forces of the spine (muscle and gravity wise) are in an axial compression as well as in a ventral direction, parallel to gravity, sustaining an equilibrium [42]. These anterior load vectors create stability in the vertebrae of the spine. The mentioned changes of the upright position made anterior shear loads diminish, directing the loads (gravity and muscle wise again) in vectors that act in opposite directions. Certain vertebrae of the spine are located in a place in space where anterior vectors are no longer existent. These forces are then replaced by dorsally directed shear loads that drive the vertebra away from the anterior gravity line (Fig. 3), leading to rotational instability of the exposed human vertebrae [43].

The unique human sagittal profile

The sagittal profile of the spine plays an important role in determining the rotational stability of certain areas of the spine. During growth, the spine moves from a complete kyphosis, at intra-uterine and early neonatal stage, to an S-shaped sagittal profile in adulthood creating kyphotic and lordotic segments [44]. The axis of rotation of normal dorsal vertebrae lies in front in the vertebral body, so in an anteriorly inclined environment, shear loads fall anteriorly, increasing vertebral stability against rotation [45] (Fig. 4A). However, if the vertebrae display a posterior inclination, the axis of rotation shifts posteriorly, and posterior shear loads further move the center of rotation closer to the facets, then the vertebrae become unstable against rotation [43] (Fig. 4B). For this reason, if a sector of the spine shows backward inclined segments, it becomes more vulnerable to fail with posterior forces, and posterior directed shear forces may lead to vertebral rotation and scoliosis (Fig. 4F).

Spine development during growth

Spine evolution differs between age and sexes [46]. Females in general mature earlier than males, and the acceleration phase of rapid growth coincides with a period in which the spine is more backwardly inclined [46, 47] (Fig. 4E). This posterior inclination (usually located in the lower thoracic and upper lumbar segments, Fig. 3) further shift spinal loads posteriorly, leaving that segment with less rotational stability (Fig. 5). This may explain why initiation and progression of AIS are more prevalent in girls around puberty than in boys, who are already in a more kyphotic and anteriorly inclined phase at that stage (in whom Scheuermann kyphosis is more predominant).

Spine evolution during growth also affects the development of the discs and their mechanical properties. The spine grows predominantly through the vertebral bodies.

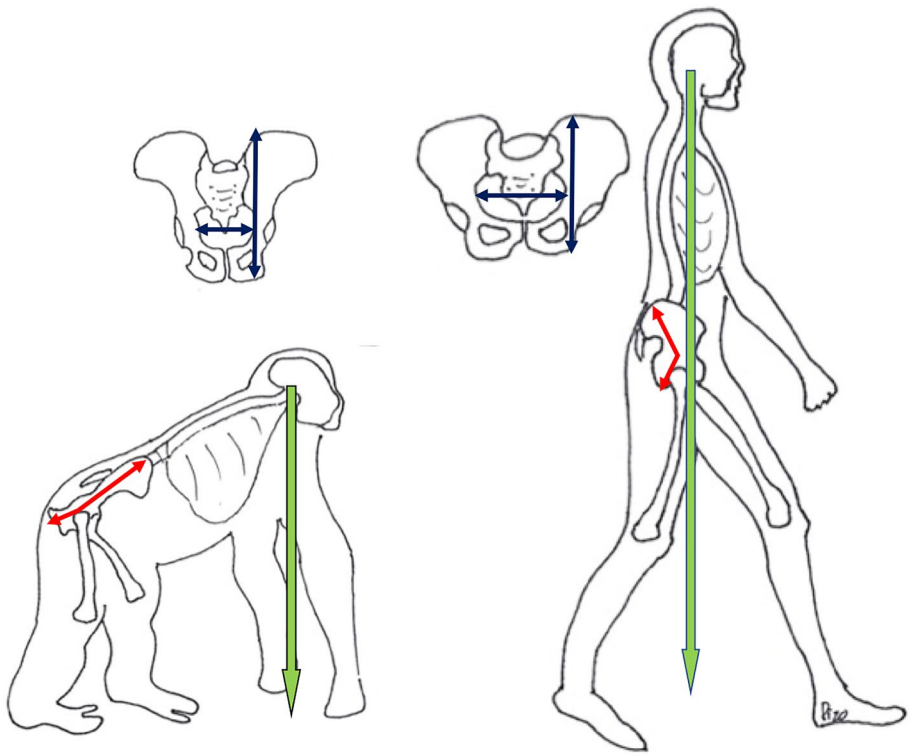

Fig. 2 Apes evolution into homo-sapiens showing changes occurring in the pelvis, spinal intersegmental loads and in the loads of gravity. Blue arrows show the changes in pelvic height and width, red arrows the change in ischio-iliac angles, and in green the center of mass force vectors

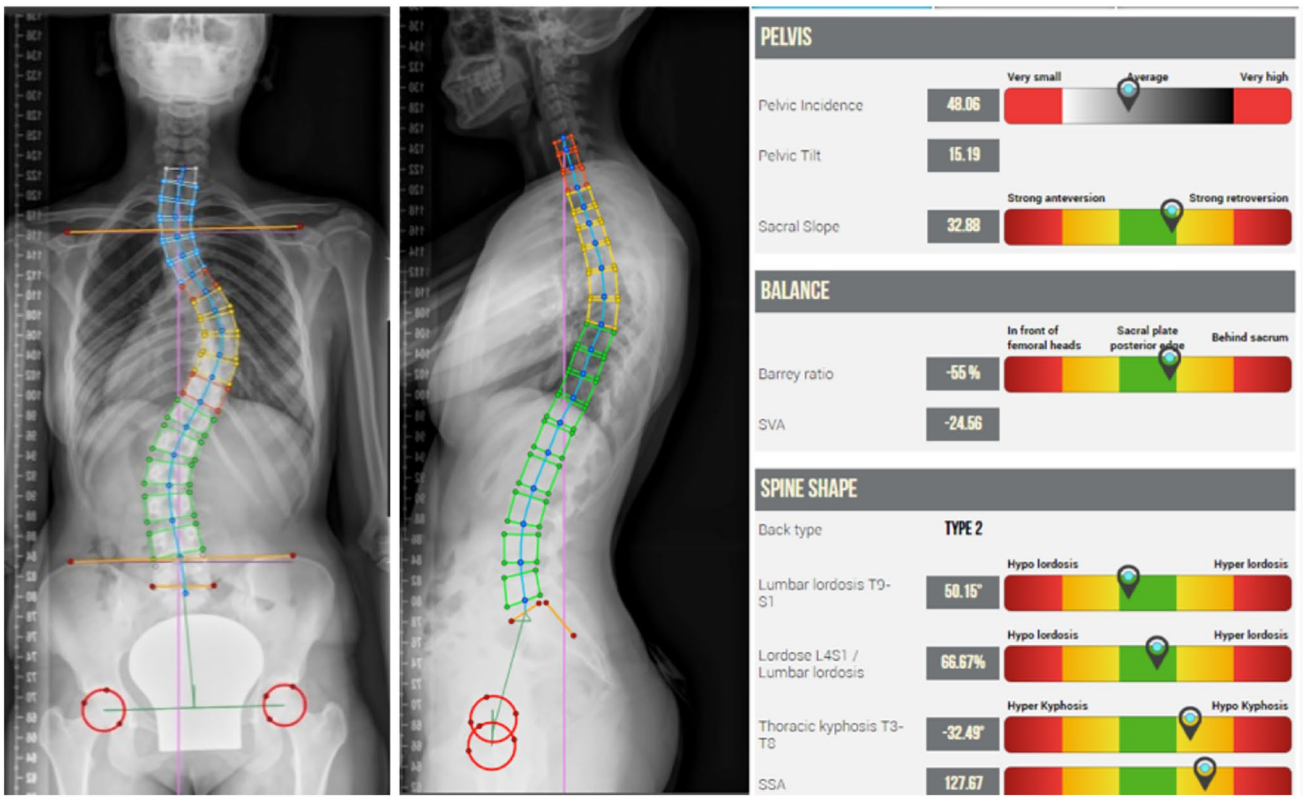

Fig. 3 The T9-L2 segment of the spine is backwardly inclined at the moment of peak height velocity, dorsally directed shear loads drive the vertebra away from the anterior gravity line creating rotational instability

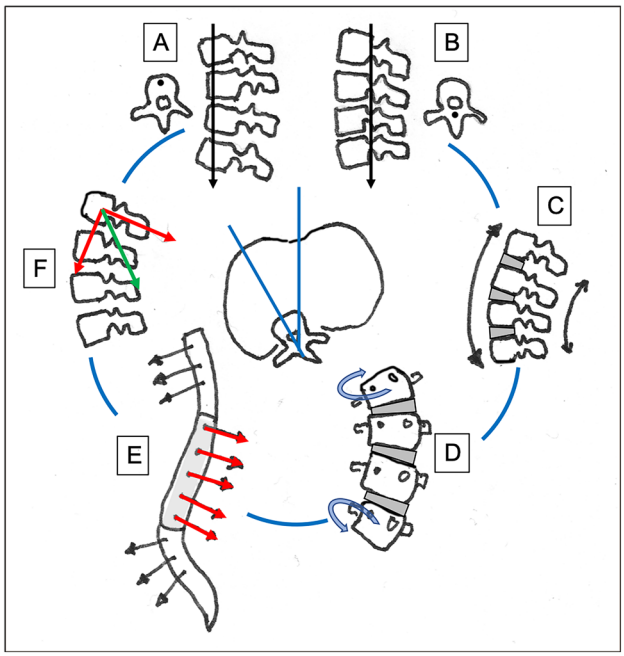

Fig. 4 The center of the image shows a preexisting axial plane rotation. **A** Segments of the spine with anterior load vectors, anterior (stable) axis of rotation. **B** Posterior load vectors shift the axis of rotation posteriorly (unstable). **C** Anterior spinal overgrowth seems to occur mostly around the apex and especially in the intervertebral discs. **D** Changes in the structure and properties of the disc during growth may impair its resistance to the different loading vectors especially rotation. **E** The acceleration phase of rapid growth coincides in females with a period in which the spine is more backwardly inclined. **F** Dorsally directed shear loads drive the vertebrae away from the anterior gravity line

The disc matures by ossifying its insertion in the vertebra through the Sharpey fibers into the initially cartilaginous ring apophyses, eventually fusing itself to the vertebral body. Thoracic disc height increases initially and then the transverse surface area increases decreasing disc slenderness [48]. By these segmental attachments to the vertebral body, the disc represents the most important stabilizer of the spine, and in the apical segment of a deformity, the intervertebral disc seems to be an important contributory factor in curve progression [49]. Changes in the structure and properties of the disc during growth or during degeneration in adulthood may impair its resistance to the different loading vectors especially rotation [50] (Fig. 4D), disturbing the natural equilibrium and predisposing to alignment failures. Apparently, deformity could start in the disc area and metabolic development characteristics can impact soft tissue (disc and ligaments) and bone quality. Actually, idiopathic scoliosis initially increases through disc wedging during the rapid growth spurt with progressive vertebral wedging occurring later [51].

Rotational instability

Scoliosis demonstrate changes in all three planes in space: axial, coronal and sagittal [52, 53]. Up to now, it has been very difficult to elucidate which plane is the initiator of scoliosis. However, the axial plane seems to be special [54, 55]. No quadrupeds have shown spontaneous rotation of the axial skeleton, but humans do. Non-scoliotic spines show a spontaneous thoracic rotatory pattern to the right of small magnitude related to the asymmetrical distribution of the internal organs [56]. As we have seen, the human spine's sagittal shape carrying the center of gravity straight above the pelvis makes it a rotationally unstable construct [42]. Thus, it appears that once the spine decompensates, it tends to follow that built-in rotational pattern that the spine exhibits at the time of onset [57] (Fig. 4).

One of the mechanical theories of scoliosis origin is the excess of the anterior length of the spine [58], producing a Relative Anterior Spinal Overgrowth (RASO). Anterior lengthening of the spine (where the spine is longer anteriorly than posteriorly) has been found in AIS patients [59]. This has been attributed to an asymmetrical growth between the anterior body endochondral ossification and the membranous ossification occurring in posterior structures [60]. However, there is some controversy in this topic, as some authors describe that scoliosis vertebrae have a wedged kyphotic morphology, and anterior lengthening seems to occur mostly around the apex and especially in the intervertebral disc (Fig. 4C), suggesting an adaptation to altered loading and not a primary growth disturbance [61]. Furthermore, anterior growth is not unique for idiopathic scoliosis, it also occurs in scoliosis with a known origin (neuromuscular, and congenital and traumatic compensatory curves), suggesting that it is part of the mechanism, rather than its cause.

Current biomechanical theory

Dickson [62] in the 80's, with his theory of biplanar asymmetry [63], speculated that thoracic lordosis developed in children with a coronal plane asymmetry and a previously rotated spine in the transverse plane [57] triggered a spinning moment that further increased spinal rotation [58]. In his theory, a flattening of the kyphosis was essential.

Nowadays, Castelein proposes a theory [43] (Fig. 4) supporting that a preexisting axial plane rotation [64], together with a rotational instability probably linked to failure constrains in the immaturity period [57], most probably coming from immature intervertebral discs [50], couples with a posteriorly inclined sagittal plane [46] that shifts the axis of vertebral rotation posteriorly, displacing the loads from an anterior to a posterior position, and this dorsal directed shear loads initiate scoliosis deformity.

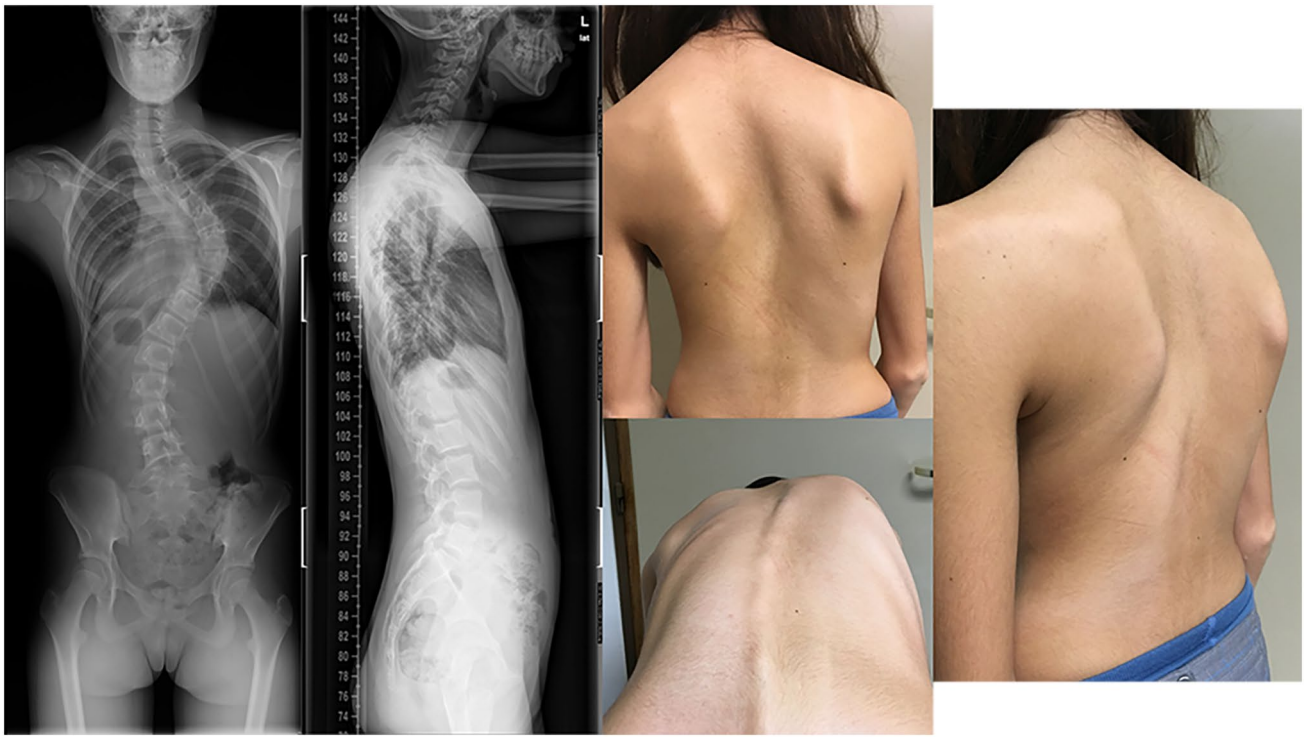

Fig. 5 Right thoracic main curve in an adolescent female. The sagittal plane shows a posteriorly inclined low thoracic segment in the radiographs, and a thoracic hypokyphosis in the clinical images

Once the three dimensional deformity starts, it progressively enters in the vicious cycle described by Stokes [65], both for the discs but also the bone. The progression of the deformity increases coronal vertebral body wedging as a result of asymmetric muscle activation and loading, eventually affecting vertebral body growth by disturbing the endplate physes.

We need, however, to remember that these biomechanical theories coexist with other mentioned hypothesis of AIS etiologies that include: genetics, epigenetics, and neurological, endocrine and metabolic dysregulations, which are also areas that merit further investigation.

Conclusion

In this article, we review the biomechanical traits of human posture, and the proposed theories that explain the special characteristics present in idiopathic scoliosis. The current biomechanical theory supports that dorsally directed shear loads acting on a preexisting axial plane rotation, in a posteriorly inclined sagittal plane of a growing patient, together with disc maturation, collagen quality at this phase of development and immaturity of proprioception, is the perfect scenario to spark rotational instability and create the three-dimensional deformity that defines idiopathic scoliosis.

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Author contributions JP, D-GC, S-IS and EI have done: Substantial contributions to the conception and design of the work, acquisition, analysis, or interpretation of data. Drafting the work and revising it critically for important intellectual content. Final approval of the version to be published and JP, D-GC, S-IS and EI agree to be accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature.

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Data availability It is a literature review article, data shown here comes from the references compiled in the text. No patient raw data was used.

Declarations

Conflict of interest Javier Pizones declares that he has no conflict of interest. Dong-Gune Chang declares that he has no conflict of interest. Se-Il Suk declares that he has no conflict of interest. Enrique Izquierdo declares that he has no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Institutional review board statement As it is a review article, it did not need Institutional Review Board Statement, it was not applicable.

Informed consent Not applicable.

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