REVIEW

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School scoliosis screening, a program useful not only for the prevention of scoliosis. Part two: a clinical research tool for the study of the aetiology of idiopathic scoliosis.

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ABSTRACT

This report presents the contribution of the school scoliosis screening program on aetiology/scoliogeny of idiopathic scoliosis. A number of issues are discussed related to the analysis of collected data from scoliosis school screening , namely the study of the influence of environmental factors in IS prevalence, that is the geographical latitude, menarche and the role of melatonin in IS pathogenesis, the relevance of scoliosis in women with visual deficiency, the age at menarche and its relation to laterality of the curve, the role of the brain in truncal asymmetry and idiopathic scoliosis pathogenesis, the thoracic cage in normality and its role in IS pathogenesis. We present the introduction of segmental thoracic ratios method and of the segmental Rib Vertebra Angles and Rib Vertebra Angle Differences in thoracic radiographs. The relative narrowing of the chest during growth: a hypothesis involving pelvic and thoracic inertia in gait and the introduction of double rib contour sign and the Rib Index. The impact of the lateral (sagittal plane) spinal profile, the role of the intervertebral discs in IS pathogenesis and the association of cavus foot with IS are also discussed. Additionally, the analysis of the somatometric parameters, the study of surface topography and the role of leg length inequality are presented. A pathophysiologic concept possibly common with IS is postulated studying the BMI in relation to the asymmetrical healthy adolescents. The parental age at birth is presented as a possible epigenetic factor/mechanism for the truncal asymmetry of a child. Finally, we summarize the outcomes and the hypothesized concepts related to IS scoliogeny, resulting from our SSS program, and our related publications on all the above discussed topics.

KEYWORDS: school scoliosis screening, aetiology, idiopathic scoliosis, environment, IS prevalence, geographical latitude, menarche, melatonin, IS pathogenesis, visual deficiency, age at menarche, curve laterality, brain, truncal asymmetry, thoracic cage, segmental thoracic ratios, segmental rib vertebra angles, segmental rib vertebra angle differences, growth, thoracic inertia, gait, double rib contour sign, rib index, lateral spinal profile, sagittal plane, intervertebral disc, cavus foot, somatometric parameters, surface topography, leg length inequality, BMI, epigenetics, parental age, IS concepts.

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"Mother nature created the spine articulated and mobile and we have to take any effort to keep it like this"

Introduction

The knowledge of normality is necessary for the study of abnormality. In this context the school scoliosis screening (SSS) programs serve the study both of these conditions, that is the study of normality and abnormality in children and adolescents during growth. Through the implementation of SSS programs data of growing school children and adolescents are collected and analyzed. Consequently, the axiom that the anatomy/morphology, may express/reflect and decipher/decode the physiology and pathology is used to clarify possible "paths" related to the understanding the scoliogeny.

At the beginning of our SSS program in 1997, we examined not only children of the ages according to the existing policies, that is approximately children from 9-14 years of age, when 85% of clinically significant IS appear [1,2], but we also screened pupils/students from 6 - 18 years old, namely from the first elementary grade [5-6 yrs. of age] to the last grade of high school [17-18yrs of age]). The beneficial result of this policy was that we had a great opportunity to collect data from a wide age range of the examined school children and adolescents.

The original main aim of the SSS programs is to identify most or all the individuals with unrecognized idiopathic scoliosis (IS) at an early stage when a less invasive treatment is more effective, in other words it is prevention. Beyond its original aim, SSS programs provide the opportunity for collection of various cross-sectional data, a) of normal children of general population [high, weight, menarche, handedness etc.] and b) similar data of asymmetric/scoliotic children and adolescents. These programs also enable the comparison of normals to asymmetric/scoliotics children and adolescents. Therefore, SSS programs are a "human evidence- based" "clinical research" tool of IS aetiology-scoliogeny based on the study of humans not animals, based on the above-mentioned axiom of the association of the anatomy/morphology to physiology/pathology.

The SSS offered information for the epidemiology and natural history of adolescent IS (AIS), [3,4]. Analysis of our domestic SSS programs, performed at the various cities of Greece, documented the national incidence of IS, and the estimation of the probable number of children who will need to be conservatively or surgically treated, [5,6].

During the years 1975 - 1999, 17 School Screening programs were performed in Greece and their results were analyzed and published in the book " School Screening in Greece", [2]. From the data of 1998 Hellenic National Census, the population of children aged 8 to 14 years old was approximately 751.000. With the above - mentioned datum and with a national mean IS incidence of 2.9%, (Cobb angle ≥ 10°), 21.779 children were expected to have scoliosis of variable severity. 980 of them would need conservative treatment using a brace, while 41 children would need surgical treatment, [5].

The examination of the role of the industrial environment on IS prevalence in the industrialized region revealed that prevalence was similar to this observed in other non-industrialized geographical departments of the country. This implies that industrial environmental factors probably do not significantly influence the prevalence of AIS, [7].

Further in this report the outcomes of our SSS program are summarized and the contribution of these studies on aetiology/scoliogeny of IS, Table 1.

1. Study of the influence of environmental factors in IS prevalence (geographical latitude), menarche and the role of melatonin in IS pathogenesis.

In the international peer review published literature, the IS prevalence is dissimilar in various geographic latitudes, namely higher values are reported in northern countries. The regression of prevalence of IS of each place by the latitude of the place where each study was conducted, was found statistically significant ($p < 0.001$). This observation could be related to the influence of the geography of a specific region on human biology and could be affected by socioeconomic and environmental factors such as temperature, humidity or light, [8, 9].

The above finding was documented using peer review reports of IS prevalence in countries only of the norther hemisphere. Currently we encourage

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TABLE 1.

Contribution of the SSS program on aetiology/scoliogeny of idiopathic scoliosis (IS)
a. Study of the influence of environmental factors in IS prevalence (geographical latitude) and the role of melatonin in IS pathogenesis
b. prevalence of scoliosis in women with visual deficiency
c. age at menarche in IS girls and its relation to laterality of the curve
d. the role of the brain in trunk asymmetry (TA) and IS pathogenesis
e. thoracic cage in normality and its role in IS pathogenesis/scoliogeny
f. the impact of the lateral spinal profile (LSP), (sagittal plane)
g. the role of the intervertebral discs (IVD) in IS pathogenesis
h. association of cavus foot with IS
i. anthropometric data in IS patients
j. SSS referrals and surface topography (ST)
k. SSS referrals and Leg Length Inequality (LLI)
l. Study of the BMI in relation to the TA of healthy adolescents, a pathophysiologic concept possibly common with IS
m. Parental age at birth as a possible epigenetic factor/mechanism for the TA of child

similar studies in the southern hemisphere counties in order to confirm the results. The initial findings show that countries further southern from the equator like Chile, have increased value of IS prevalence, [10]. Similar studies are now organized and being contacted in Brazil and Indonesia, countries that extend from the equator and much further south.

In peer review published literature the menarche is reported to be different in places of various geographic latitudes, namely in higher values in northern countries. Consequently, we hypothesized a possible association between prevalence of IS and age at menarche among normal girls in various geographic latitudes, [11].

The regression of prevalence of IS and age at menarche by latitude documented for each study, was found statistically significant ($p < 0.001$) and both were following a parallel ascending course of their regression curves, especially in latitudes northern than 25 degrees. This means that late age at menarche is matching with higher prevalence of IS, a finding which was not reported earlier in the available to us peer review literature.

Melatonin, "the light of night", is secreted from the pineal gland, principally at night. Among other biological functions, the hormone is involved in the sexual maturation of females, [12]. Melatonin acts in gonads indirectly, reducing the secretion of gonadotropins and mainly the luteinizing hormone (LH), [13]. The menarche is related with episodic secretion of LH during the night, [14, 15]. Melatonin may play a role in the timing of puberty and the onset of puberty in humans may be related to the decline in melatonin secretion that occurs as children grow, [16]. We hypothesized that the amount of light, which is different in different geographical latitudes influences melatonin secretion and alters age at menarche. Delayed puberty results in a prolonged period of spine vulnerability when other aetiological factors are contributing to the development of IS, [11]. Furthermore, we found that this positive association between prevalence of IS and geographic latitude is present only in girls and not in boys. This contradictory association implicates that the possible role of environmental factors acts in a different way between boys and girls, [8].

The role of melatonin deficiency in IS pathogenesis was proposed after development of scoliosis similar to those of human's IS in pinealectomized chickens, [17]. Fagan et al, 2009, reported that caution is advised when drawing conclusions regarding the pathogenesis of AIS from this model, [18]. Several other publications argued that there is a controversy whether chickens are appropriate models for studying scoliosis, because they present extrapineal sites of melatonin production that contribute to circulating melatonin levels, in contrast to humans that no extrapineal sources affect the circadian rhythm of melatonin. Melatonin's actions appear to differ between humans, other mammals, and other vertebrates, [19,

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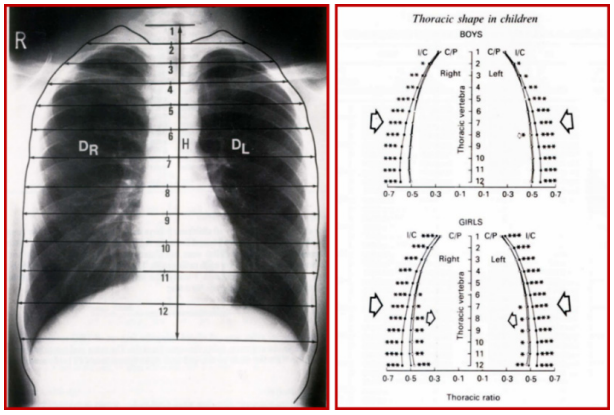

Figure 1. *Left figure - Chest radiograph to show the method of measurement for calculation of thoracic ratios (TR) fromT1-T12. DR (DL) = distance measured from midpoint of the distal end-plate of each vertebral body (Tl- 12) to the outline of the lateral border of the right (left) thoracic cage. H = distance from Tl- 12. Right figure - TRs for infancy (I), childhood (C) and puberty (P). (Modified from Grivas et al 1991). [38].*

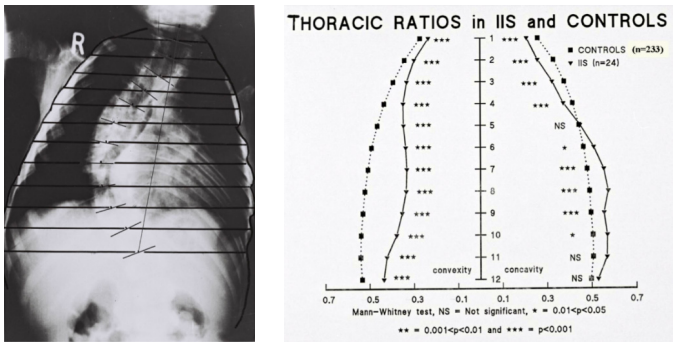

Figure 2. *In IIS the thoracic cage is under-developed compared to non-scoliotic counterparts. (Modified from Grivas et al 2006), [34].*

20, 21, 22, 23]. Also, pinealectomy in bipedal nonhuman primates did not produce scoliosis in any of the 18 monkeys examined in a mean follow up period of 28 months, [24]. Furthermore, no increased IS prevalence has been observed in children after pinealectomy or pineal irradiation because of pineal neoplasias, although they have a lack of serum melatonin in the majority of studies, [25, 26, 27].

2. Prevalence of scoliosis in women with visual deficiency.

Girls with visual deficiency were found to have a delayed age at menarche (13 years old versus 12.58 years of controls) and their prevalence of IS was found to be much increased (42.3%). This is strongly supporting the hypothesis that in blind girls, the lack of light through the increased levels of melatonin may delay sexual maturation and expose for longer period the growing immature spine to detrimental causative factors of IS, which result in increased IS prevalence, [28].

3. Age at menarche and its relation to laterality of the curve.

The age at menarche in IS girls is reported to be delayed, compared to nonscoliotic girls. This generalized statement questions the accuracy of reported records for age at menarche which are found different at different geographical latitudes. Our findings, derived from our SSS program referrals in Greece, didn't show any statistically significant difference of the age at menarche between scoliotic and non-scoliotic girls, [29]. Additionally, analyzing the laterality of the curve in relation to age at menarche we found that premenarchal IS girls presented predominantly with a left primary scoliotic curve, while postmenarchal IS girls presented predominately with a right primary scoliotic curve [30]. This observation which associates the age of IS onset with the laterality of the curve requires further investigation and this finding would not be figured out without running a SSS program, [30]. Both of the above-described findings (no different menarchial onset of the non-IS and IS girls and the different laterality of the curves in pre and post menarchial IS girls) were confirmed in a recent research study in Serbia and Bosnia – Herzegovina, areas with almost similar geographical latitude with Greece, [31]. As known, in infancy when boys develop IS, they are more frequently presented with left sided thoracic curves. Our finding on laterality of curves in pre-menarchial scoliotic females, revealed by the analysis of data of the referred children from SSS, justifies the hypothesis that the pre-menarchial developed left curves may be due to the same mechanisms/causes with those functioning for the more frequently developed left thoracic curves in infant IS males. This finding may be due to the impaired development of

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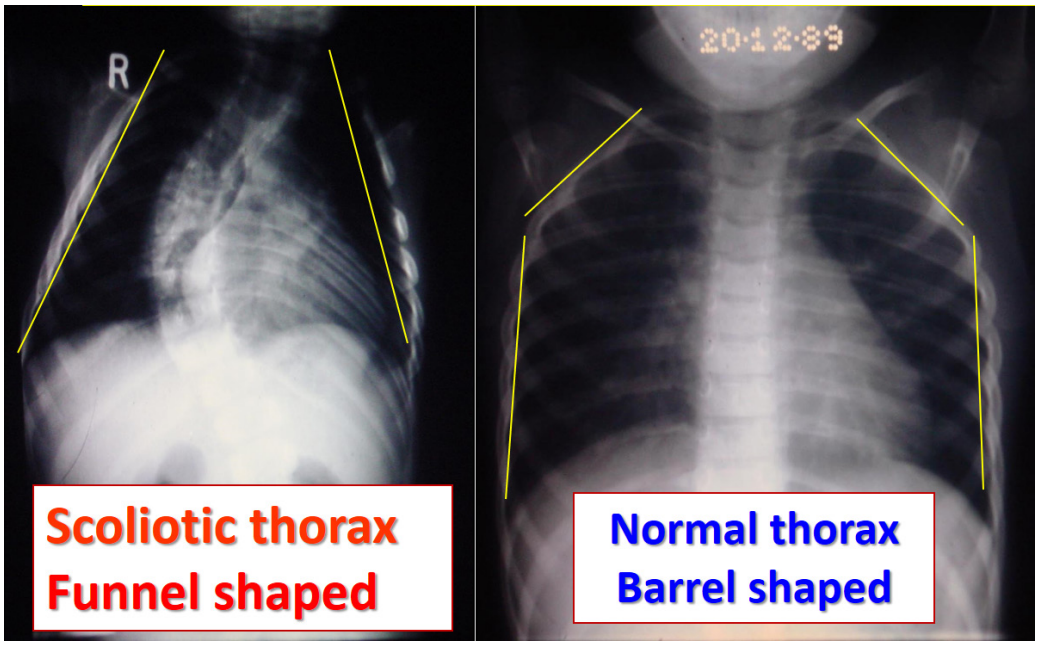

Figure 3. *The thorax in IIS is funnel shaped compared to the thorax in controls which is barrel shaped.*

the infantile scoliotic thoracic cage, but this suggestion needs more investigation, [32, 33, 34, 35].

4. The role of the brain in TA and IS pathogenesis.

The analysis of the data for truncal symmetry and asymmetry using the scoliometer, collected from our SSS program, from symmetric controls and asymmetric children showed that there is a significant correlation of mild mid-thoracic asymmetry to the dominant brain hemisphere in terms of handedness, in children who are entitled at risk of developing IS, [36, 37].

5. The thoracic cage in normality and its role in IS pathogenesis/scoliogeny

The introduction of segmental thoracic ratios (TR) method in thoracic anteroposterior radiographs. This new segmental thoracic ratios (TR) radiographical method of segmentally assessment of growing normal thorax from T1-12, was conceived and presented by the author, [38]. On each chest radiograph, the outline of the lateral border of the thorax is drawn, (Figure 1). Next, the midpoint of the distal end-plate at each vertebral body from Tl- 12 is marked. Then, at each segment, the distance from the middle of the end-plate to the outline of each of the right and left thoracic cage is measured. These distances are standardized by dividing by the measured T1- T12 distance. They are termed segmental right and left thoracic ratios (TRs). Ratios are also calculated segmentally for the total width of the chest (right plus left measured lengths).

The TR method was used to study the thorax of infantile IS (IIS), and compare it with this of controls, figures 2. Using the segmental TRs method it was shown that in IIS the thoracic cage is under-developed compared to non-scoliotic counterparts. The thorax in IIS is narrower than that of the controls, the upper chest is funnel-shaped, figure 3, and there is a predictive value of the vertebral rotation* at the upper limit of the thoracic curve of IIS, that is the vertebral counter-rotation at T4 predicts the apical vertebral rotation at follow-up, which reflects impaired rib control of spinal rotation possibly due to neuromuscular factors, which contribute also to the funnel-shaped chest, (*compared with specific rotation of Perdriolle and Vidal - the so called "specific angle of rotation". In an anteroposterior roentgenogram, specific rotation (RS) is the sum of the rotation in the axial plane of the two vertebrae adjacent to the superior end vertebrae). [32, 39, 40, 41].

The introduction of the segmental of Rib Verte-

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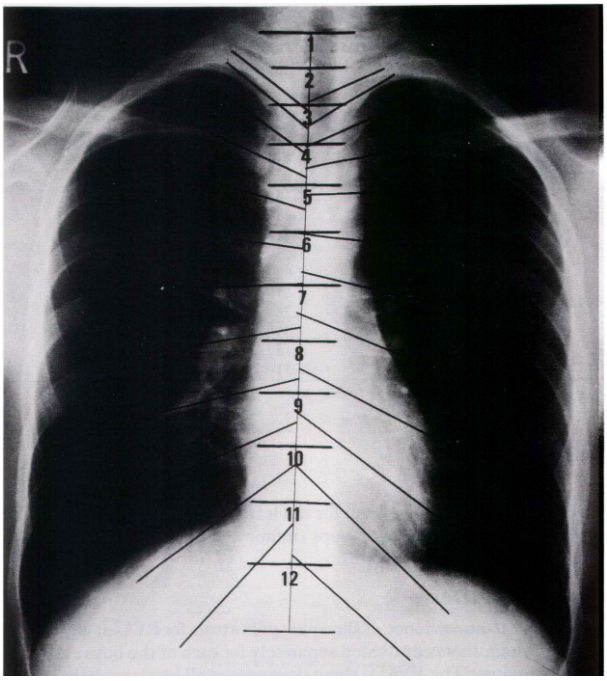

Figure 4. *Segmental rib-vertebra angles from T1-T12, (modified from Grivas et al 1992).*

bra Angles (RVAs) and Rib Vertebra Angle Differences (RVADs) in thoracic anteroposterior radiographs, (figures 4,5,6).

The apical RVA and RVAD was initially (1972), presented by Mehta, [42]. This radiographical method of segmental RVAs and RVADs from T1-12, was for the first time presented for the study of the growing normal thorax, [37], (Figure 4, 5, 6).

The RVAs are a functional index which is visible on the chest radiographs. It was suggested that the differences of the RVAs between right and left side is the expression of asymmetric muscle forces acting on the thoracic cage, which deforms early and possibly transfers the deforming forces to the spine. It is concluded that that measurement of the RVAs, whether as apical RVAD or as segmental RVAs gives early information about the process of curve initiation and progression. Significantly asymmetric RVAs have been observed even at Cobb angles of 8°, i.e. before the diagnosis of scoliosis is made, [43].

Segmental Rib vertebra angle difference (asymmetry) (RVAD) in controls.

Left RVA minus Right RVS mean in degrees

Comparing the RVAs between the mild late onset IS (10—20 Cobb degrees) and nonscoliotic children, it is shown that the late onset IS children rib cage had lower RVAs, that is the thorax is narrower. This indicates that the scoliotic thorax is under-developed compared to non-scoliotic counterparts, [44], Figure 7.

During growth the thorax remodels. The drooping of the lower ribs of girls, which is more evident than in boys, occurs between infancy and childhood, or largely before the girl's pelvis increases in size, [37, 38, 44, 45, 46, 47a, 47b, 48].

Relative narrowing of the chest during growth: a hypothesis involving pelvic and thoracic inertia in gait.

We postulated a hypothesis, namely that the mechanism by which this rib droop occurs is through neuromuscular factors. Between childhood and puberty, the increased rotational inertia generated by the larger pelvis of girls is not associated with further lower rib drooping but, we suggest, with rib growth impairment (relative to spinal growth) in the lower half of the chest. During the same developmental period (childhood to puberty), boys show no further relative narrowing of the chest, [49, 50].

Also, our hypothesis is that the relative diminution of TRs particularly of the lower thorax with increasing age in boys and girls may be a mechanism to reduce the rotational inertia created in the thorax from the rotating thoracolumbar spine and pelvis in gait, [51, 52]. Such a mechanism would conserve energy. It will be recalled that inertia (I) equals Σmr^2, (where Σ =sum, m= mass and r = radius). Hence, a relative diminution of thoracic width would produce a much greater reduction of rotational inertia, because inertia is a function of the square of the distance. In evolutionary terms, the chest narrowing is consistent with an adaptation of the human ribcage to bipedal gait. This hypothesis suggests that RVA drooping, as a mechanism to narrow the chest for mechanical reasons (energy conservation), can go so far; below a certain RVA droop, rotation control of the spine would be compromised. To avoid this situation in girls, rib growth is impaired in order to narrow the lower thorax further between childhood

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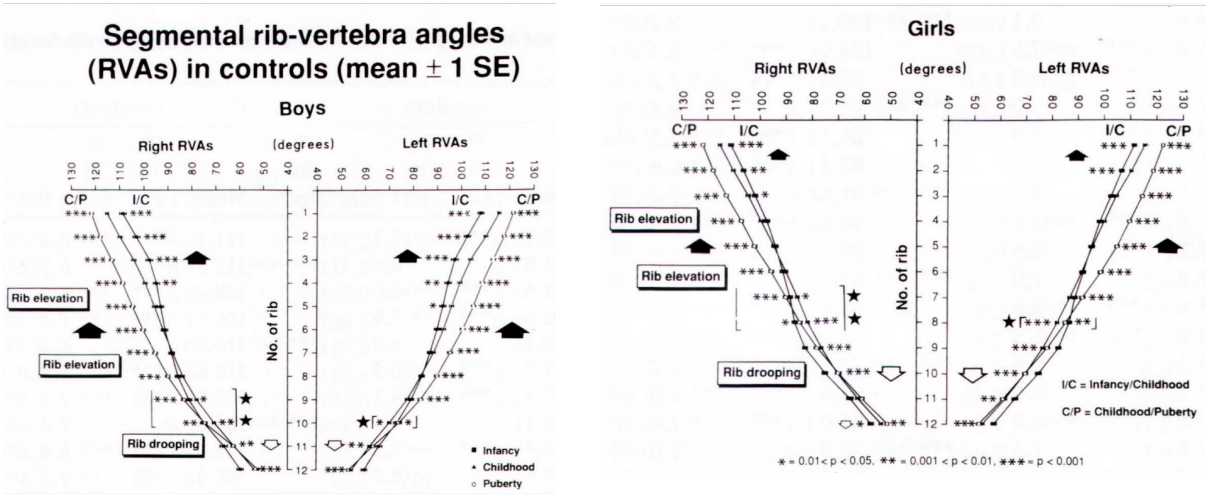

Figure 5. *Segmental rib-vertebra angles (RVA's in degrees) in boys and girls for each of the infancy (I), childhood (C), and puberty (P) groups by rib level. (modified from Grivas et al 1992).*

and puberty to lessen the rotational inertial burden, [37].

The introduction of double rib contour sign (DRCS) and the Rib Index (RI) (Fig. 8).

This sign and index were initially presented in Greece during the 25th "Nicolas Giannestras-Panayiotis Smyrnis" Anniversary Symposium of Spinal Column Diseases, at the Porto Rio Hotel, Patras, Greece, 21-23 May 1999, [53]. Later it was presented in the International Research Society of Spinal Deformities meeting at Clermont Ferrand, Château du Marand, France, 23-26 May 2000, [54], and it was published in 2002. This publication focused on the implications of DRCS on the aetiology of idiopathic scoliosis, [55].

All lateral spinal radiographs in IS show a DRCS of the thoracic cage, a radiographic expression of the rib hump (RH), Figure 8. The outline of the one hemi-thorax (convex) overlies the contour of the other hemi-thorax (concave). Then the rib index (RI) method extracted from the DRCS was introduced in order to quantify the severity of the double rib contour (DRC) that is to evaluate the rib hump deformity, in IS patients in an attempt to create a safe reproducible way to assess the RH deformity based on lateral radiographs. This assessment actually represents the appraisal of the transverse plane rib-cage deformity, a method applied to the lateral spinal radiographs. The application of Rib index is useful for documentation of the thoracic deformity before any treatment, the assessment of physiotherapy treatment, the assessment of brace treatment and the pre- and post-operative assessment of the rib-cage deformity correction on the transverse plane, [56].

The effect of growth on the correlation between the spinal and rib cage deformity.

Growth has a significant effect in the correlation between the thoracic and the spinal deformity in girls with idiopathic scoliosis. Using the RI as an expression of the thoracic deformity and Cobb angle as an expression of the spinal deformity, the existence of any correlation between these two parameters was tested. Linear association was seen only between thoracic Cobb angle and rib-index in the age group of 14–18 years. (Predicted Thoracic Cobb Angle = - 6.357 + 7.974 × (Rib-Index). Figure 9. This new finding was very interesting as it implicated that in younger children the thoracic deformity and the spinal deformity are not associated but only in older children, [57]. Dr Smyrnis 2000, seven years ago, observed this phenomenon based on his clinical experience only and noted it in his lecture published in the cited book, [2], that is "the most critical

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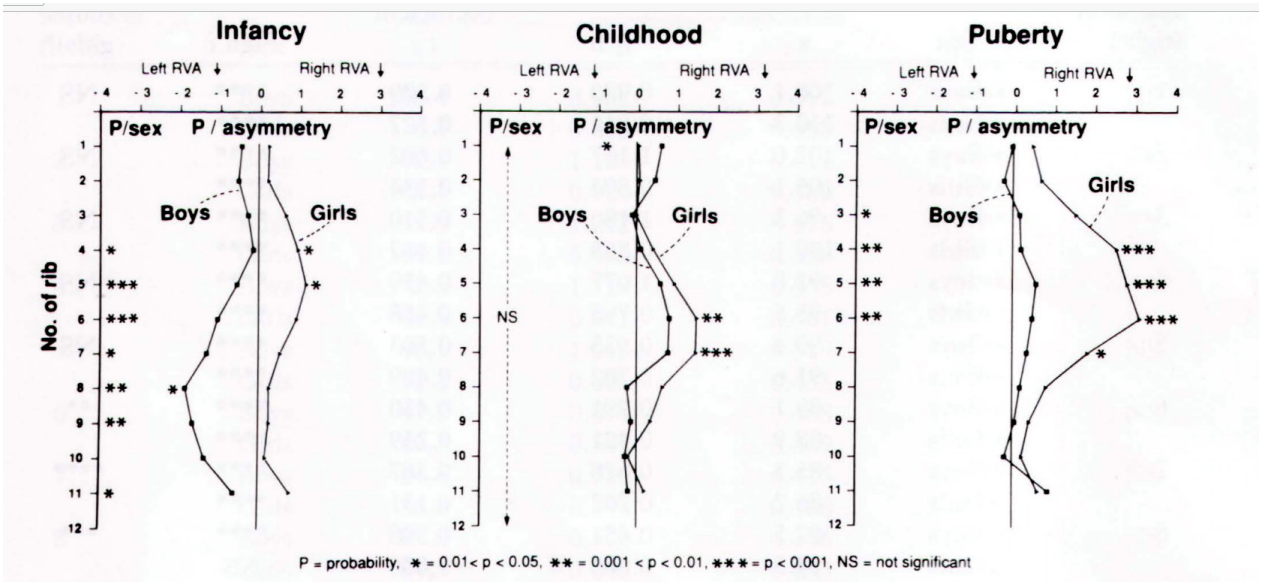

Figure 6. *Segmental rib-vertebra angle asymmetry (rib-vertebra angle difference, RVAD) in the "normal" boys and girls for each of the infancy (I), childhood (C), and puberty (P) groups. Overall, the pattern of this " normal" RVA asymmetry reflects the age, sex, and laterality patterns of IS. It suggests that extremes of RVADs may be etiological factors for both infantile and AIS. (Modified from Grivas et al 1992).*

age for mass screening is from 10-13 years old, and in this cohort of ages it is usually observed 3:1 ratio between clinically and radiologically positive children".

Growth seems to have a significant effect in the correlation between the rib cage and the spinal deformity in girls with IS. The findings of this study support the hypothesis that the correlation between thoracic surface and spinal deformity is weak in younger children, implicating that the thoracic cage deformity precedes that of the spine in the pathogenesis of IS, [57, 58].

6. The impact of the lateral (sagittal plane) spinal profile (LSP).

In a study of children, referred from our SSS program, suffering mild (10-20 degrees) IS, it was found that the LSP in thoracic spine hypokyphosis is not a predisposing aetiological factor. This was concluded because in the initiation of IS curves the LSP is similar to that of their healthy controls, [59]. This study provides evidence that thoracic hypokyphosis by alleviating axial rotation is rather a compensatory mechanism than an aetiological factor of IS pathogenesis, figure 10.

The above finding was confirmed in a recent study of the LSP of the spine in IS using the surface topography, scoliometric assessment and the radiographical imaging, [60]. Thus, it is clear that hypokyphosis is not a primary causal factor for the commencing of mild or moderate IS curve, but it could be considered as a permissive factor in the scoliogeny, [60], figure 11.

7. The role of the intervertebral discs (IVD) in IS pathogenesis.

In the postero-anterior radiographs of mild IS children referred from our SSS program, it was shown that the deformity appears first at the level of the IVD, which is found wedged. The deformity of the vertebral body in spinal column follows. The deformation of the apical IVD and its adjacent IVDs seems to be an important progressive factor in IS pathogenesis, [61, 62], figure 12.

8. Association of cavus foot with IS.

It is well known, that in a number of certain neuromuscular diseases cavus foot and scoliosis are

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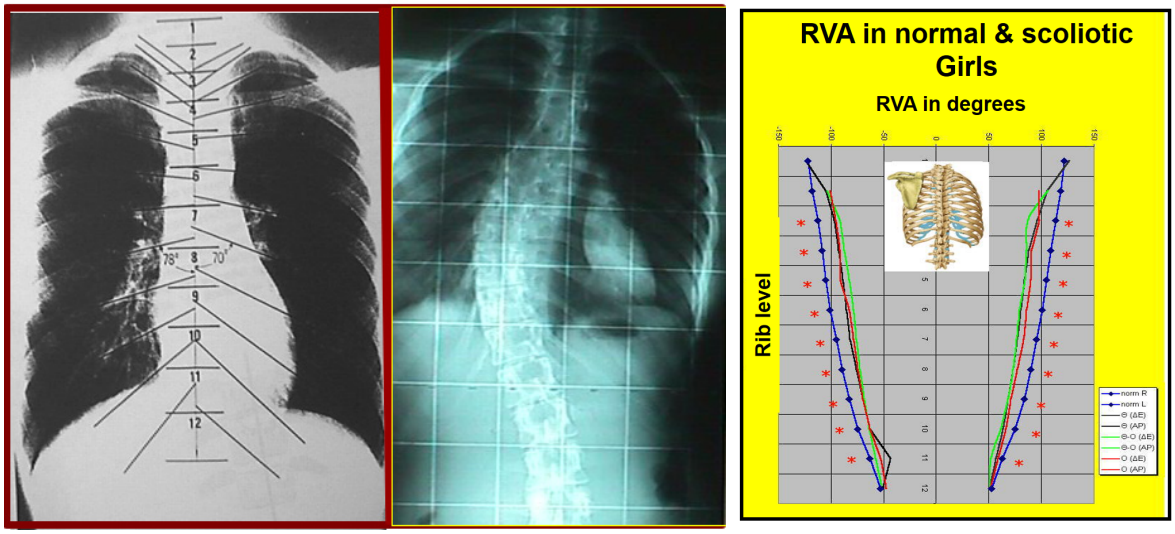

Figure 7. *The scoliotic thorax is under-developed compared to non-scoliotic counterparts. (Modified from Grivas et al 2002), [44].*

presented together. Such diseases are muscular dystrophy, cerebral palsy, Friedrich's ataxia, Charcot-Marie-Tooth disease, poliomyelitis, syringomyelia or spinal cord tumors. Having in mind this observation many authors studied the relationship between foot morphology (especially pes cavus) and scoliosis, as it was supposed that these pathologic conditions may share a common cause.

During the first 13 years (1996 – 2009) of our Thriasio Hospital SSS program implementation we also contacted foot printing. The Harris–Beath mat for foot-printing was used. We investigated if there is a relationship between cavus foot, type 1 of footprint [84], figure 13, and IS in a population referred from our SSS program. The significant correlation between IS and cavus foot as it has elsewhere been reported was not verified in our study. No positive correlation was found between IS and flat foot [84], type 6 of footprint, figure 13, as well in our study, [63, 83].

9. The somatometric parameters.

Analysis of our SSS program collected data yielded the somatometric parameters and comparison of these parameters of nonscoliotic children with their counterparts suffering mild IS. The scoliometer readings in both standing forward bending position (StFBP) Adam's test and sitting forward bending position, (SiFBP) test of 2071 children and adolescents (1099 boys and 972 girls) aged from 5 to 18 years old were studied. The mean frequency of TA of 7 or more degrees was 3.23% for boys and 3.92% for girls at the StFBP and 1.62% and 2.21% at the SiFBP, respectively. Girls are found to express higher frequency of TA than boys. Right TA was more common than left. The sitting position is the preferred screening position for examining the rib or loin hump during school screening as it demonstrates the best correlation with the spinal deformity exposing the real TA, [64]. The cross-sectional study of TA using the scoliometer, in normal juveniles provides data which describe the evolution of TA, from early childhood to adolescence. Juveniles were found more symmetric than adolescents, who were studied previously in a different study. Furthermore, juvenile girls were found more symmetric than boys. Juvenile TA pattern seems to be in accordance with the higher incidence of juvenile IS in boys. Furthermore, severe TA, which could be correlated with a scoliotic curve, was found to be more common to the left side. These reports provided information about the variability of back morphology in normal juveniles. The amount of TA detected in children during SSS, which may reveal a spinal curve, is the main indicator/marker for referral and further orthopaedic assessment but

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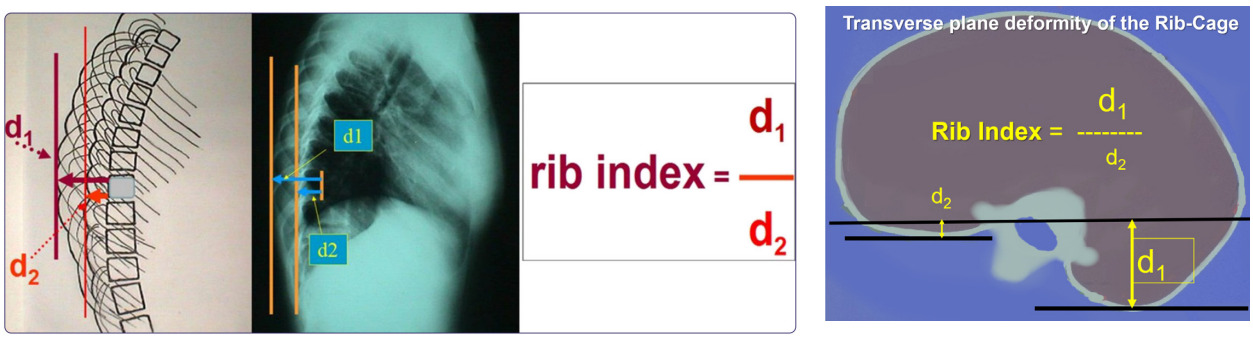

Figure 8. *The DRCS and the RI in the lateral thoracic radiographs used for the thoracic transverse plane deformity assessment, (Modified from [56]).*

can also be used as a baseline for further research on IS aetiology, [65, 66].

The creation of a database of the collected data with somatometric parameters, i.e. of body weight and height from the entire cohort of the SSS program children provided the opportunity to compare these parameters of nonscoliotic children with their counterparts suffering IS with curves of a Cobb angle 10 degrees. In our studied Mediterranean sample of the population, the somatometric parameters of height and weight in children with mild IS, regardless of curve type and site, were not found statistically different from their nonscoliotic counterparts, [67].

10. SSS referrals and surface topography (ST). (Figure 14).

The evaluation of the effects of the Adam's standing forward bending position (StFBP) test versus the standing erect (SE) position on back TA was conducted using the scoliometer readings in the Adam's StFBP and the 4D Formetric (the Diers surface tomography apparatus 4DF; Diers International, Schlangenbad, Germany) readings in the SE position. It was shown that back TA in children and adolescents differs in the StFBP and 4DF Erect (SE) positions. This is probably attributed to the complicated truncal anatomy, and the results of this study may be used as a useful foundation for further understanding of torso dynamics, [68].

11. SSS referrals and LLI.

In children and adults LLI may affect their posture, gait, and several truncal parameters, and it can cause scoliosis. In our study we assessed truncal and spinal changes due to mild LLI using ST analysis. The LLI was statistically significant correlated to the 4DF, reading of pelvis rotation, pelvic tilt (pelvic obliquity), and surface rotation. The scoliometer readings of ATR/ATI in the lumbar region were statistically significant correlated to the 4DF readings of pelvic tilt (pelvic obliquity). The normally symmetric truncal parameters were also statistically significant changed, all these deviating from the line of gravity through the vertebral prominence. Interestingly, LLI was not statistically significant correlated to the scoliosis angle and the scoliometer reading at the lumbar level, [69].

12. Study of the BMI in relation to the TA of healthy adolescents, a pathophysiologic concept possibly common with IS.

Studying the somatometric data collected from children examined in our SSS program, their body mass index (BMI) was calculated, that is the measure of body fat based on height and weight) and consequently we formulated the following hypothesis. This hypothesis suggested that the pathogenesis of severe TA in girls and boys, has the same mechanism as that proposed for AIS girls, namely: severe TAs are initiated by a genetically-determined selectively increased hypothalamic sensitivity (up-regulation, i.e. increased sensitivity) to leptin, with asymmetry as an adverse response to stress (hormesis), mediated bilaterally mainly to the growing trunk via the sympathetic nervous system (leptin-hypothalamic-sympathetic nervous system

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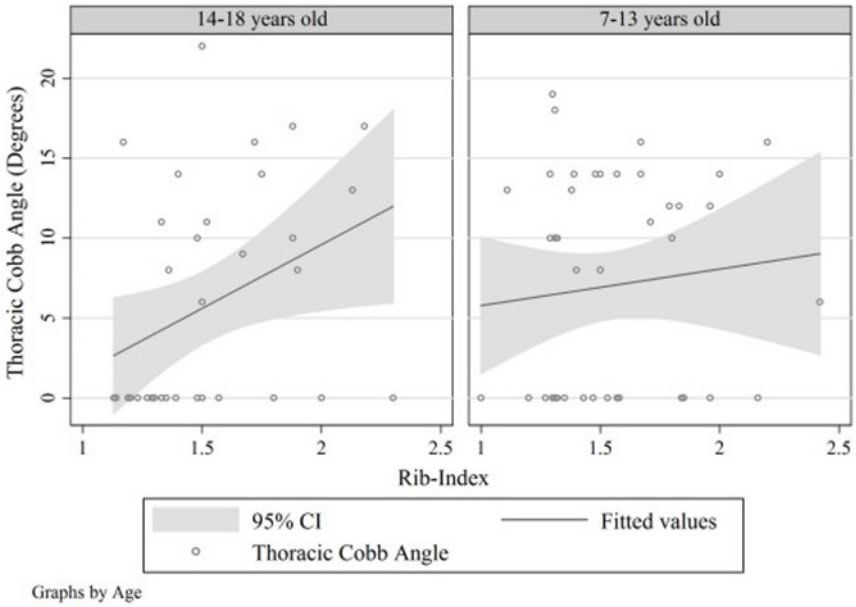

Figure 9. *A linear association was the one between Thoracic Cobb Angle and rib-index in the age group of 14–18 years not in younger aged girls. This implicated that in younger children the thoracic deformity and the spinal deformity are not associated but only in older children. (Predicted Thoracic Cobb Angle = -6.357 + 7.974*(Rib-Index). [57].*

(LHS) concept), [70].

13. Parental age at birth as a possible epigenetic factor/mechanism for the TA of child.

Parental age at birth is implicated as a possible epigenetic mechanism for the in TA of a child [71, 72, 73, 74]. The age of the mother as an environmental factor in the general population may potentially influence epigenetically the onset of TA in boys more than girls as well as during growth. The significance of the findings is based on the principle that the endometrial environment is vital to the planning of the fetus for health and illness throughout its life, [75, 76, 77]. Consistent findings reported from the USA, Edinburgh and Sweden reveal increased maternal age as a risk factor for AIS, suggesting maternal factors can predispose to it, [78 ,79, 80]. It seems that males are more affected by this factor but, unexpectedly in our study, by younger and not older mothers as reported for AIS in the literature, [81, 82].

It is very interesting to note that this clinical research on IS aetiology based on SSS is the only "Human evidence based" research contributing to our understanding of IS scoliogeny and we solidly recommend it.

In conclusion, the outcomes and the hypothesized concepts related to IS scoliogeny, resulted from our SSS program and the study of the imaging of non-IS and IS growing thoracic cages are outlines.

1. The amount of light, which is different in different geographical latitudes influences melatonin secretion and alters age at menarche. Delayed puberty results in a prolonged period of spine vulnerability when other aetiological factors are contributing to the development of IS, the prevalence of which varies in different geographical latitudes.
2. In norther geographical latitude the IS prevalence is higher.
3. The prevalence of IS is higher in females with Visual Deficiency.
4. Premenarchal IS girls present predominantly left primary scoliotic curve, while post-menarche IS girls present predominately right primary scoliotic curve
5. There is a significant correlation of mild

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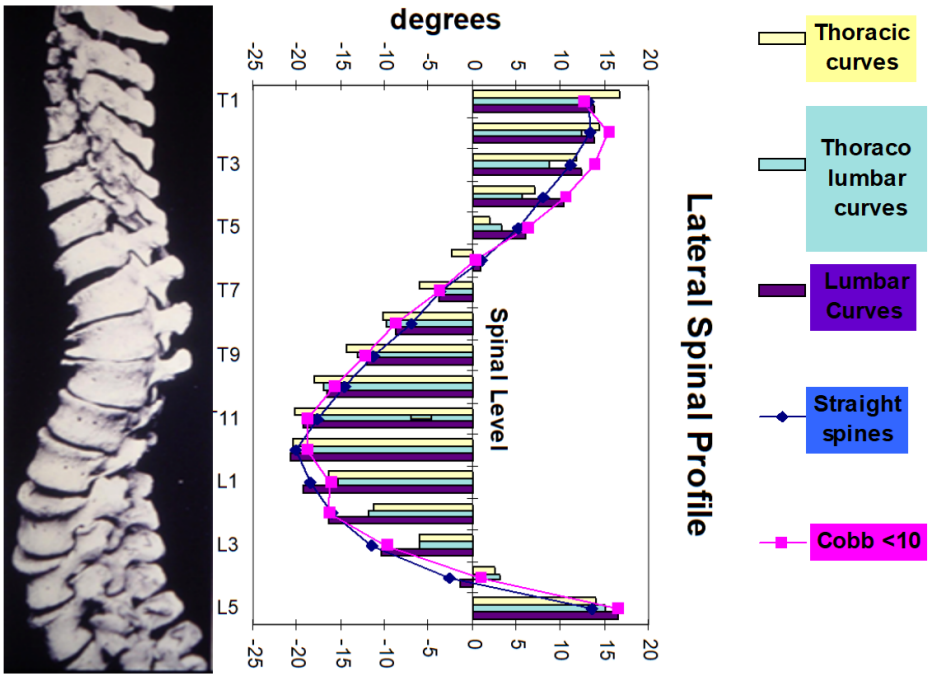

Figure 10. *The LSP in children with 1) straight spines, 2) with spinal curvature having a Cobb angle less than 10°, and 3) in scoliotic children with a) thoracic, b) thoracolumbar and c) lumbar curves. Comparing the children's LSP between the above groups, using Mann-Whitney test, it was shown that no statistical difference was noticed, in almost all spinal levels. (Modified by Grivas et al 2002, [59]).*

mid-thoracic asymmetry to the dominant brain hemisphere in terms of handedness, in children who are at risk of developing IS.

6. Introduction of the segmental thoracic ratios method assessment of thorax in thoracic anteroposterior radiographs.

7. Introduction of the segmental of RVA and the segmental RVAD method for assessment of the growing thorax in thoracic anteroposterior radiographs.

8. The pattern of "normal" segmental RVAD in "normal" boys and girls for each of the infancy, childhood, and puberty groups, reflects the age, sex, and laterality patterns of IS. It suggests that extremes of RVADs may be etiological factors for both infantile and AIS.

9. The thorax in IIS is funnel shaped compared to the thorax in controls which is barrel shaped.

10. During normal growth the thorax remodels. There is drooping of the lower ribs both in boys and girls. The drooping of the lower ribs of girls, is more evident than in boys.

11. The relative narrowing of the lower chest during growth: a hypothesis involving pelvic and thoracic inertia in gait. The relative diminution of TRs and RVA particularly of the lower thorax with increasing age in boys and girls may be a mechanism to reduce the rotational inertia created in the thorax from the rotating thoracolumbar spine and pelvis in gait.

12. The introduction of DRCS and the RI. RI is used for a. the documentation of the thoracic deformity, b. assessment of physiotherapy, c. assessment of brace treatment and d. pre- and post-operative assessment; of the rib-cage deformity correction on the transverse plane.

13. The effect of growth on the correlation between the spinal and rib cage deformity. In younger children the thoracic deformity and the spinal deformity are not associated but only in older children.

14. The impact of the LSP, (sagittal plane). The LSP, (hypokyphosis) is not a primary causal factor for the commencing of mild or moderate IS curve, but it is a permissive factor for the scoliogeny.

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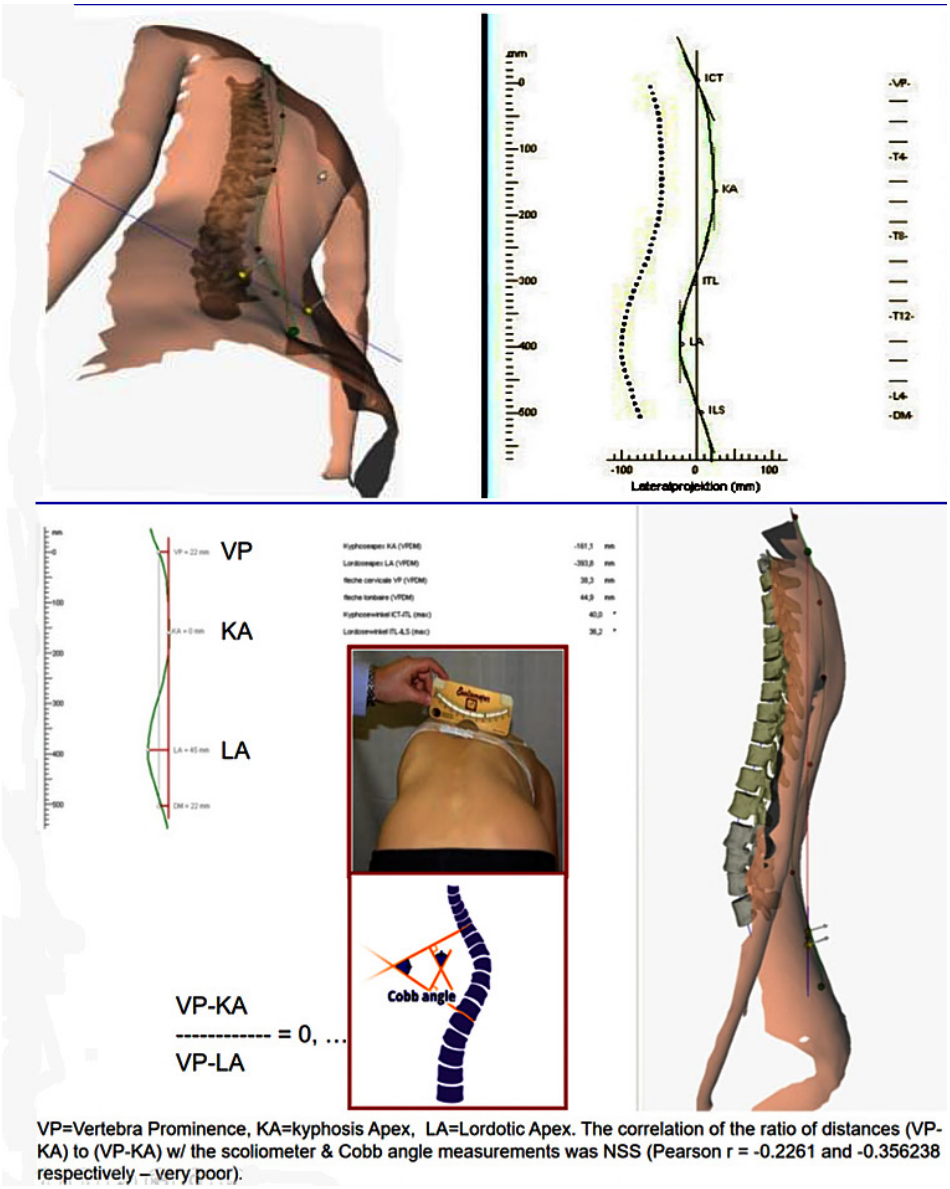

Figure 11. *Study of the sagittal profile of the spine in IS using surface topography. (Modified by Grivas et al 2021, [60]).*

15. The role of the intervertebral discs (IVD) in IS pathogenesis. The deformity appears first at the level of the IVD. The deformity of the vertebral body in spinal column follows.

16. There is no association of cavus foot and IS.

17. The somatometric parameters. Girls are found to express higher frequency of TA than boys. Right TA is more common than left. The sitting position is the preferred screening position for examining the rib or loin hump during SSS as it demonstrates the best correlation with the spinal deformity exposing the real TA.

18. SSS and ST. TA in children and adolescents differs in the StFBP and 4DF Erect (SE) positions. This is probably attributed to the complicated truncal anatomy, and the results of this study may be used as a useful foundation for further understanding of torso dynamics.

19. LLI and ST. LLI is not statistically significant correlated to the scoliosis angle and the scoli-

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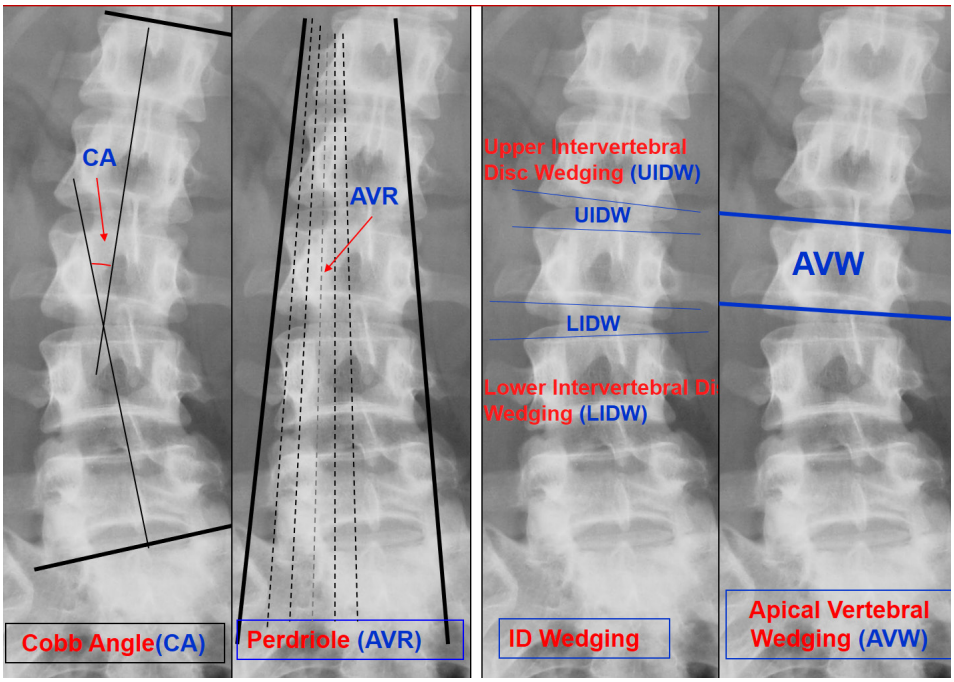

Figure 12. *The deformity appears first at the level of the IVD. (Modified by Grivas et al 2021, [61, 62]).*

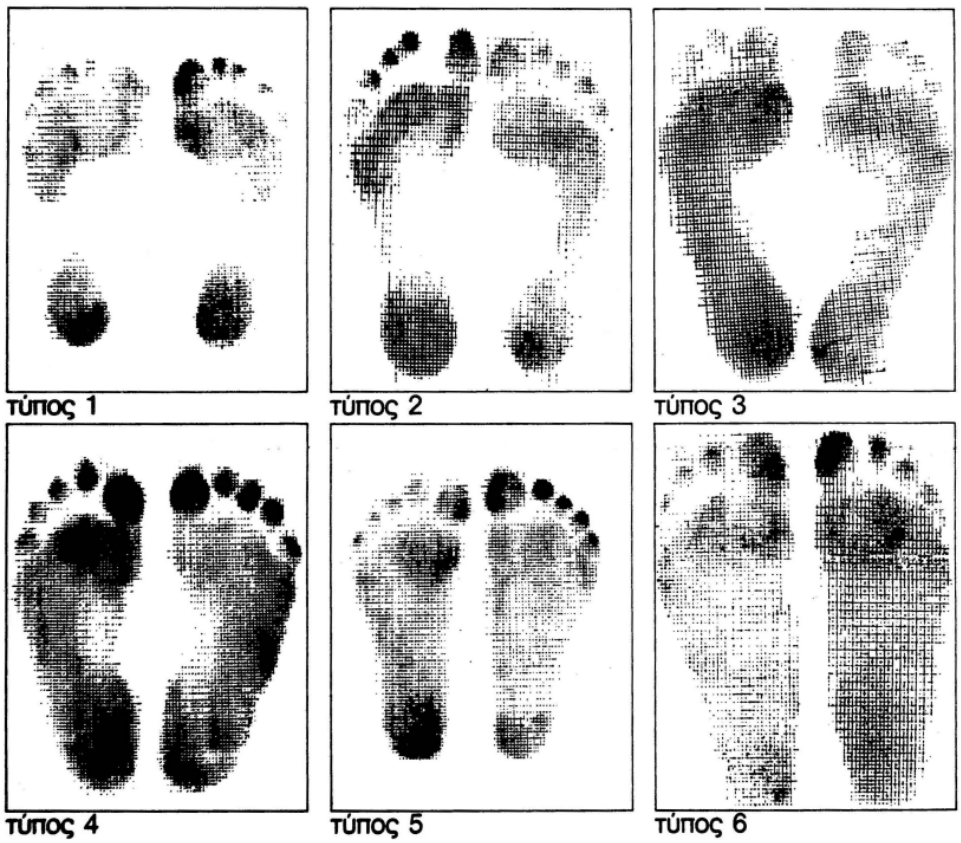

Figure 13. *The footprint type 1, of cavus foot, according to the 6 types of footprints, (Grivas 1984 [83]), was not associated with IS.*

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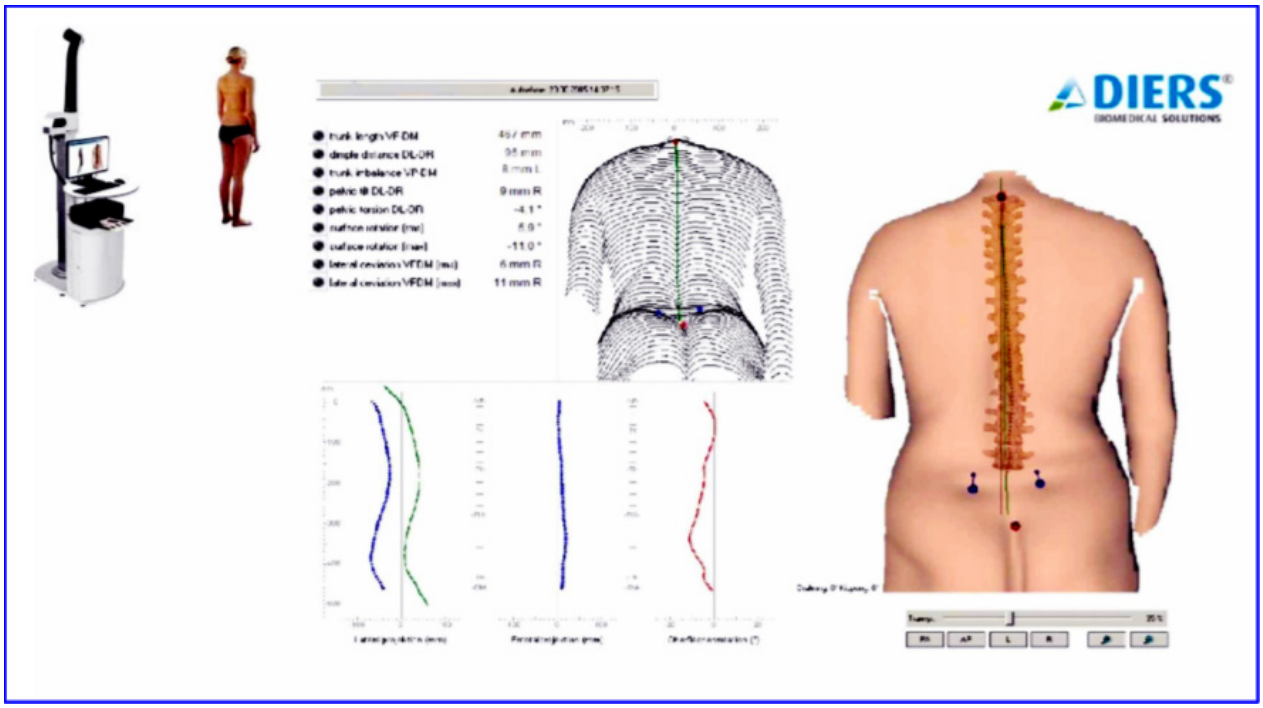

Figure 14. *Study of the LLI in children suffering mild IS using the 4DF apparatus. (Modified from [68]).*

ometer reading at the lumbar level TA in children and adolescents.

20. We postulated a hypothesis studying of the BMI in relation to the TA of healthy adolescents: we suggested a pathophysiologic concept possibly common with IS.

21. The parental age at birth is an epigenetic factor/mechanism for the TA of child. Males are more affected by this factor, if born by younger and not older mothers.

Abbreviations

ATI = angle of truncal inclination
ATR = angle of truncal rotation
AIS = Adolescent Idiopathic Scoliosis
BMI = body mass index
DRCS = double rib contour sign
IS = idiopathic scoliosis
IIS = Infantile Idiopathic Scoliosis
IVD = intervertebral discs
AIS = adolescent idiopathic scoliosis
LLI = Leg length inequality
LHS = leptin-hypothalamic-sympathetic
RI = Rib Index
RVA = Rib Vertebral Angle
RVAD = Rib Vertebral Angle Difference
StFBP test = forward bending position test
SiFBP = sitting forward bending position,
SSS = School scoliosis screening
SE = standing erect
ST = surface topography
TA = trunk asymmetry
TR = thoracic ratio
4DF = 4D Formetric

Competing interests

The author declares that he has no competing interests.

Author's contribution

The author was responsible for organizing the SSS program and the examination team, managed the administration of it, involved in the examination of children, conceived and postulated the described concepts written in this report, implemented the literature search and drafted this manuscript.

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