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Original Article

The first study of epidemiology of adolescent idiopathic scoliosis shows lower prevalence in females of Jammu and Kashmir, India

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Abstract: AIS is a heterogeneous 3D spinal deformity with Cobb angle ≥10°. It affects children in the age group of 10-16 years globally with 2-3% prevalence and significant female predominance. The exact etiology of AIS is not known however, it is supposed to be associated with factors such as anthropometric, metabolic, neuromuscular abnormalities and genetics. Objectives: To determine the prevalence of AIS and association of anthropometric factors with AIS in the studied population group. Methodology: Scoliosis screening of 9,500 individuals was carried out at different educational institutions of Jammu region in Jammu and Kashmir, India using a scoliosis-meter. The subjects were later examined radiologically. Results: In population of the region, AIS was most prevalent among all types of scoliosis with overall prevalence of 0.61%. The prevalence was observed to be lower in females (0.31%) than males (0.88%). Based on angle of trunk rotation (ATR), lumbar curves were more prevalent than thoracic curves. Average Cobb angle in males and females were 24.9° and 22.6°, respectively. BMI showed significant association with AIS in the age group of 12-16 years (*P* value =0.028). Furthermore, height was significantly associated with AIS in the overall screened population (*P*-value =0.029). Conclusions: The AIS patients in the Jammu region of India have unique clinical features. In contrast to the global prevalence data, the prevalence of AIS in females in the region was less in comparison to males. Based on epidemiological literature and our findings, we hypothesized that genetic factors might be a major contributor in the AIS pathogenesis along with other confounding factors such as height, BMI, ethnicity, etc.

Keywords: Adolescent idiopathic scoliosis, prevalence, Cobb angle, BMI, angle of trunk rotation, Jammu and Kashmir

Introduction

Adolescent idiopathic scoliosis (AIS) is a common spinal disorder that develops between 10 to 16 years of age and is characterized by a lateral curvature of spine with Cobb angle of more than 10°. There has been a wide variation in the prevalence of AIS in different populations of the world. The prevalence of AIS in general population lies between 2-4% [1]. Globally, AIS is more prevalent in females than in males with female/male ratio of 1.5 to 11 [2]. About 2-3% adolescent population have scoliosis with a Cobb angle of greater than 10°, 0.3-0.5% population with a Cobb angle of more than 20°, and less than 0.1% of the population have severe scoliosis, i.e., with a Cobb angle of more than 40° [3]. The prevalence of the AIS varies with

the geography [2] and it is reported more in the northern latitudes than in the lower latitudes [4]. However, the incidence varied in different studies and populations of the world [5-14].

Despite being idiopathic there are several factors related to the possible etiology of AIS including hormones, biomechanics, anthropometric, metabolic, growth and neuromuscular abnormalities [15]. In addition to this, AIS is strongly considered to be associated with the genetic factors [16]. For centuries, the underlying genetic, cellular and molecular basis of AIS has remained uncertain. However, new approaches to genomics and system biology are helping to illuminate the genetic modifications underlying AIS risk [2]. The AIS heritability is indicated by its higher prevalence in the first degree relatives of individuals with scoliosis within a family than in general population and by the twin studies that show its higher concordance rate in the monozygotic twins than in dizygotic twins [3, 17, 18]. Certain genes that were identified with the pathogenesis of AIS on the basis of GWAS, whole-genome and exome sequencing as well as candidate gene approach include *LBX1, GPR126, BNC2, CHL1, PAX1* and others, alike [19-25]. Candidate gene association studies have reported many genes which may play a functional role in the development of AIS. Some of the candidate genes that were evaluated for the susceptibility of AIS were supposed to be involved in different pathways like bone formation and bone metabolism, connective tissue structure, puberty and growth hormones, neurological and melatonin signaling pathways [26].

Early detection of AIS helps in preventing further progression of scoliosis in an individual either by non-surgical (bracing) or by surgical methods [27]. For early detection, school-based screening is an effective method and is recommended by the American Academy of Pediatrics, American Academy of Orthopaedic Surgeons and the Pediatric Orthopaedic Society of North America [28]. The Adam's forward bend test and scoliometer measurement are used for scoliosis screening. The latter gives the angle of trunk rotation (ATR). The individual is considered to be scoliotic if the scoliosis meter reading is ≥7°, and the final confirmation for scoliosis is done by radiographic diagnosis [4].

The annual scoliosis screening of all school aged children (preferred between 12-18 years) has been recommended by the Scoliosis Research Society (https://www.srs.org/) [4] and is a common practice in most developed countries. However, in India, so far, prevalence of scoliosis has been reported from only two small geographical regions (0.13% in Patiala city of Punjab and 0.2% in Assam) [29, 30].

Lack of epidemiological studies on scoliosis explains its unawareness and ignorance in India. The present school screening study was performed in 125 educational institutions comprising 9,500 individuals to determine the prevalence of the AIS in Jammu region of India by using Adam's forward bend test and radiological verification. Further, it was examined that whether or not the prevalence of scoliosis was influenced by gender in our population. We have also evaluated the possible association of AIS with anthropometric factors such as BMI, height and weight.

Materials and methods

Preparatory work

The study was approved by Institutional Ethics Review Board (IERB), Shri Mata Vaishno Devi University (IERB serial no: SMVDU/IERB/18/69) and communicated to Human Genetics Research Group (Figure S1). For carrying out awareness of scoliosis in target population, simplified brochures were designed which contained all the relevant information about scoliosis including its causes and consequences. Screening camps at different districts of Jammu region were held in collaboration with registered non-government organizations.

The parents of the children were informed a week before the screening by means of letters regarding the intentions of the study, its significance and the method of screening and diagnosis. Additionally, school authorities were also provided with the datasheet and consent form so as to get their consents and to have an idea about the parameters and the information collected during screening. Prior to the screening at schools, briefing up of the screening process and the details required during screening were properly demonstrated to the students.

Scoliosis screening program

The screening was carried out by the team of university researchers, trained in measuring

Table 1. Prevalence of scoliosis in the Jammu and Kashmir population

Gender	No. of Individuals screened	No. of Scoliosis cases	No. of AIS cases	Prevalence of AIS (%)
Male	5,001	47	44	0.88
Female	4,499	17	14	0.31
Total	9,500	64	58	0.61

AIS: adolescent idiopathic scoliosis.

the angle of trunk rotation using scoliosis-meter (Baseline®, USA), in 120 schools and 5 higher educational institutions located in various districts of the Jammu region of J&K. The students from the age group of 10 to 28 years were screened by adopting the random sampling method. The screening was carried out in a separate room using the Adam's forward bend test, where an individual bends forward while his/her feet and hands joined together or feet kept shoulder width apart. Any asymmetry of the shoulder level or waist line was measured using scoliosis meter which ultimately gives the ATR.

Information about age, gender, ethnicity, family history, ancestral place and anthropometric measurements (including height, weight and BMI) of the children were collected. The status of neurological, muscular or skeletal diseases was also recorded. The angle of trunk rotation of 7° was taken as the cut off value for the scoliosis.

Radiological examination

The individuals with ATR ≥7° were referred to the hospitals for the confirmation of the condition by radiological examination. Allis test was done by clinicians to rule out any functional scoliosis that may arise because of leg length discrepancy followed by the X-ray of the complete pelvis to look for any malformation or injury in the pelvic region. Antero-posterior and lateral X-rays of the spine were taken for the confirmation of the scoliosis. Cobb angle of 10° or more was considered to be scoliotic. Vertebral anomalies were checked in the X-ray reports to rule out congenital scoliosis.

Statistical analyses

All statistical analysis was carried out using Microsoft Excel 2013, R programming on R studio version 1.2.5033 and SPSS v.23.0. Prevalence of AIS has been evaluated in the male, female and in the overall population using Microsoft Excel 2013. To evaluate the association of different confounding factors (anthropometric factors) with AIS multiple statistical tests were performed. The independent t-test was carried out to evaluate the association of anthropometric factors including height, weight and BMI with AIS in overall screened population and in the age group of 12 to 16 years. The test was aimed to determine whether the difference in the means of the confounding factors in cases and controls were statistically significant or not. To evaluate the strong relationship between anthropometric factors (BMI, height and weight) with ATR in cases, Pearson's correlation coefficient was calculated using SPSS. The level of significance of ≤0.05 was considered as a criterion for the statistical significance for all statistical analysis. 3D scatter plot was generated using R studio to visualize the distribution of BMI in cases and controls in the age group of 12-16 years.

Results

In this study, 9,500 individuals participated in the screening program from various regions of the Jammu. There were 5,001 males and 4,499 females. The overall prevalence of scoliosis (including AIS, infantile, congenital and functional scoliosis) was 0.67%, whereas the prevalence of AIS was 0.61%. The prevalence of idiopathic scoliosis in males was 0.88%, whereas that of female was 0.31% (**Table 1**). The male/female ratio was 1.1:1 in the screened population. The population screened was ethnically diverse comprising several ethnic groups of J&K, including Rajputs, Brahmins, Scheduled Castes, Scheduled Tribes, Kashmiri Pandits and Kashmiri Muslims. We did not find association of scoliosis with any particular ethnic group.

Our study mainly focused on AIS and it was found to be more prevalent than other types of scoliosis in both males and females in this region (**Table 2**). We excluded all other types of scoliosis based on the clinical evaluation. Cases excluded from our study comprised two

Table 2. Types of scoliosis in the Jammu and Kashmir population

Gender	Types of scoliosis cases				
	No. of Infantile	No. of Congenital	No. of Kyphoscoliosis*	No. of Functional**	No. of Idiopathic
Male	1	0	1	1	44
Female	0	1	1	1	14

*With fused vertebrae along with profound kyphosis, **due to leg length discrepancy.

Table 3. Curve types of AIS in the Jammu and Kashmir population

Gender	Curve type of AIS*		
	No. of Thoracic	No. of Lumbar	No. of Double curve
Male	20	21	3
Female	5	9	0

AIS: adolescent idiopathic scoliosis. *On the basis of angle of trunk rotation.

congenital scoliosis cases where vertebral fusion was the major reason. There were two kyphoscoliosis cases having congenital vertebral anomaly with profound kyphosis, two cases of functional scoliosis who had leg length discrepancy, and also a case with infantile idiopathic scoliosis who was diagnosed at the age of 2 years and had strong family history of scoliosis (**Table 2**). Notably, AIS is less prevalent in females than in males in contrast to the data reported elsewhere in the world [2].

The lumbar curve was more prominent than thoracic curve in both males and females, whereas only three male subjects were observed to have double curve (**Table 3**). Moreover, the average Cobb angle of all individuals with idiopathic scoliosis was 25.4°. The average Cobb angle was 24.9° in males with AIS, and 22.6° in females with AIS. All the individuals who were having ATR ≥7° had Cobb angle of >10°. These results suggest that based on the Cobb angle the curvature of spine was also greater in males than in females. To evaluate the association of anthropometric factors with AIS, an independent t-test was done for factors such as, height, weight and BMI between the affected individuals and the healthy controls in overall screened population. No significant association was observed for weight and BMI among AIS patients and healthy controls, with *P*-value of 0.453 and 0.610 respectively. However, height showed significant association with AIS having *P*-value of 0.029 where the mean height was higher in cases (163.0±10.81 cm) as compared to controls (159.79±20.32 cm) in the overall screened population. As AIS develops more frequently in the adolescent age (12-16 years), in order to evaluate the possible role of anthropometric factors in the development of AIS, we narrowed down our population size by selecting the population in adolescent age group (12-16 years) from the overall population screened. The association of anthropometric factors (height, weight and BMI) with AIS in the adolescent age group was carried out using independent t-test between the affected individuals and healthy controls. A significant association of BMI with AIS has been observed with *P*-value of 0.028. The AIS patients were found to have lower BMI (mean BMI of 17.67±2.79 kg/m^2) as compared to the healthy controls (mean BMI of 19.01±4.06 kg/m^2) in the adolescent age group. However, no significant associations were observed for height and weight (*P*-value of 0.291 and 0.302 respectively) (**Table 4**). A 3D scatter plot was generated to visualize the distribution of BMI among cases and controls in 12-16 years age group (**Figure 1**). It can be clearly seen from the graph that cases are concentrated more towards lower BMI as compare to that of controls. It was observed that majority of the cases (19) were underweight (BMI<18.5) followed by 5 cases in normal weight category with BMI in the range of 18.5 to 24.9 (**Figure 1**). In this study, we have also evaluated the correlation between BMI, height and weight with ATR in AIS cases. No signification association was observed for BMI with ATR (*P*-value =0.580, r=-0.071), height with ATR (*P*-value =0.415, r=-0.104) and weight with ATR (*P*-value =0.314, r=-0.129).

Discussion

The prevalence of scoliosis varies in different populations of the world. In India, till now the prevalence has been reported only from two small geographical regions, i.e., Patiala city of Punjab and in the state of Assam. The present study is the first report conducted for the screening of scoliosis and its prevalence in the population of J&K, India. Interestingly, we

Table 4. Independent t-test between cases and controls for height, weight and BMI in the age group of 12-16 years and overall population (10-28 years)

	Age group	N (No. of samples)	Average Height in cm (± SD)	Average Weight in kg (± SD)	Average BMI in Kg/m^2 (±SD)
Cases	12-16 years	24	159.91 (±11.94)	45.04 (±7.4)	17.67 (±2.79)
Controls		5518	157.26 (±24.25)	46.64 (±10.19)	19.01 (±4.06)
Independent t-test (*P*-Value)			0.291	0.302	0.028
Cases	10-28 years	58	163.0 (±10.81)	51.86 (±12.43)	19.56 (±4.43)
Controls		9436	159.79 (±20.32)	50.63 (±12.38)	19.86 (±4.36)
Independent t-test (*P*-Value)			0.029	0.453	0.610

SD: standard deviation, BMI: body mass index.

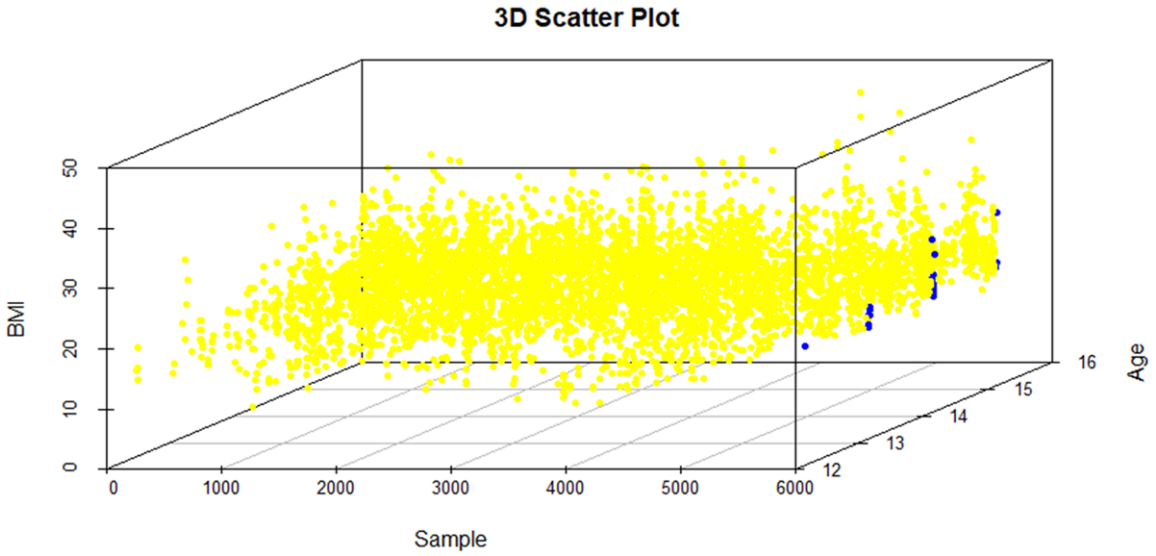

Figure 1. 3D Scatter plot depicting the BMI of all the samples including both cases and controls in the age group of 12-16 years. Cases are represented with blue dots and controls are represented with yellow dots. It can be depicted from the figure that cases are more concentrated towards the lower BMI as compared to that of controls.

observed high prevalence of scoliosis in our target region as compared to its incidence which was 0.13% in the population of Patiala, Punjab [29] and 0.2% in Assam [30]. Similarly, studies have also reported less prevalence of scoliosis in the countries such as Japan (0.87%) [31], Saudi Arabia (0.78%) [32] and Singapore (0.27-2.49% in 9-13 years old female) [33].

In our study, we also observed that individuals in the pre-obesity category had minor ATR readings, which could be due to high soft tissue content that ultimately decreases the rotational deformity measured by Adam's forward bend test [34].

In order to identify the predisposing factors of AIS, we examined the association of anthropometric factors (height, weight and BMI) with the AIS and observed the significant association of height with AIS in overall population and BMI with AIS in the children of adolescent age, i.e., 12-16 years when the AIS develops more frequently. However, the level of significance was not very high which suggested that height and BMI may act as a confounding factor for the manifestation of AIS but is not the only contributory factor for the AIS predisposition. Based on the findings reported in the literature [16], we hypothesize that genetic factors might be a major contributor in the pathogenesis of the AIS along with other confounding factors such as height, BMI, ethnicity, etc.

Conclusion

This study is the first report of AIS in the population of Jammu region, J&K, India. The preva-

lence of AIS was lower than the expected prevalence of the AIS globally with less prevalence of scoliosis in females (0.31%) than in males (0.88%). The confounding factor may not be the major contributor for the pathogenesis of AIS; instead genetics may play a major role in the AIS predisposition. The male prevalent AIS in our population could be attributed to the population structure and gene pool of the population group.

Future perspectives

As the prevalence of AIS observed in our study is contrasting to previous literature, it becomes pertinent to screen large sample size to confirm the result as well as replicate the study in another independent population group from India. Genetic studies are warranted to determine the genetic predisposition of AIS in our population group as well as to understand the cause of less prevalence of female AIS better.

Acknowledgements

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Disclosure of conflict of interest

None.

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Communication of Decision of the Institutional Ethics Review Board (IERB)

IERB Serial No: SMVDU/IERB/18/69 **Date:** 28.4.18

Project title: Genetics of Scoliosis in Indian populations
Principal Investigator: Dr. Ekta Rai
Name & Address of Institution: School of Biotechnology, Shri Mata Vaishno Devi University, Katra
☐ New review ☐ Revised review ☐ Expedited review
Date of review (D/M/Y): 12.4.2018 Date of previous review, if revised application:
Decision of the IERB: ☑ Recommended ☐ Recommended with suggestions ☐ Revision ☐ Rejected
Suggestions/ Reasons/ Remarks: As per IERB - SMVDU and ICMR Guidelines
Recommended for a period of :

Please note *

- Inform IERB immediately in case of any adverse event.
- Inform IERB in case of any major change in study procedure, site and investigator/co-investigators.
- This permission is only for period mentioned above. Annual report may be submitted to IERB.
- Members of IERB may monitor the trial if needed.

28/4/18

Signature
Member Secretary, IERB
Member Secretary
Institutional Ethics Review Board (IERB)
Shri Mata Vaishno Devi University

Figure S1. Ethical clearance certificate from Institutional Ethics Review Board, Shri Mata Vaishno Devi University.