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Original Article

Role of *LBX1* rs11190870 polymorphism in adolescent idiopathic scoliosis in the Acehnese population: A preliminary study

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Abstract

Genome-wide association studies (GWAS) have identified the single nucleotide polymorphism (SNP) rs11190870 near the *ladybird homeobox 1* (*LBX1*) gene as being associated with the susceptibility and severity of adolescent idiopathic scoliosis (AIS). However, no such genetic studies have been conducted in the Indonesian population. The aim of this study was to investigate the genetic profile of AIS patients in the Acehnese population, with a focus on *LBX1* rs11190870, and to assess its association with disease severity. A total of 30 female AIS patients were included. Genetic analysis was performed to determine the rs11190870 genotype in each subject. The association between rs11190870 and curve progression, measured by Cobb angle, was analyzed using the Mann–Whitney U test. The T allele was found to be more prevalent (73.3%), with the TC genotype being the most common (53.3%). A significant association was observed between *LBX1* rs11190870 and curve progression, where patients with the TT genotype exhibited a larger Cobb angle compared to those with TC or CC genotypes (p=0.01). This is the first study to characterize the genetic profile of AIS and its association with curve severity in the Acehnese population. These findings suggest that *LBX1* rs11190870 may act as a disease modifier in AIS. Further studies with larger sample sizes are warranted to confirm the role of *LBX1* rs11190870 in AIS susceptibility and severity in the Indonesian population.

Keywords: Adolescent idiopathic scoliosis, SNP rs11190807, *LBX1* gene, acehnese population, genetics population

Introduction

Adolescent idiopathic scoliosis (AIS), defined as a lateral spinal curvature of >10 degrees, is the most common spinal deformity found in children, affecting more females than males [1,2]. A recent systematic review and meta-analysis indicated that the prevalence of AIS was 1.68% in Asia, 1.22% in Europe, and 2.08% in South America [3]. Furthermore, this study also found that the pooled incidence of AIS was higher in females than males, 4.51% and 1.12%, respectively [3]. In Indonesia, a study in Surabaya identified a 2.93% AIS among 784 school-aged children with a female-to-male ratio of 4.7:1 [4].

Although extensive studies have been conducted on AIS, its etiology remains unclear. Several factors such as genetics, neuromuscular, hormones and metabolic dysfunction have been proposed as the plausible cause of AIS [1,5]. Previous studies have suggested that genetics play a

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significant role in the development of AIS through a complex interaction between genetic and environmental factors [6,7]. Genome-wide association studies (GWAS) have identified numerous loci as well as candidate genes associated with AIS, such as *estrogen receptor 1* (*ESR1*), *paired box 1* (*PAX1*), *ladybird homeobox 1* (*LBX1*), *G protein-coupled receptor 126* (*GPR126*), and *solute carrier family 39 member 8* (*SLC39A8*) [8]. Among the genes, *LBX1* – located on chromosome 10q24.31 – stands out as one of the most promising candidate genes in the etiology of AIS [1, 2]. A single nucleotide polymorphism (SNP) rs11190870 near *LBX1* was associated with AIS susceptibility in the Japanese [9], Hong Kong [10], and Chinese populations [5]. Previous meta-analyses also supported these findings by suggesting that the rs11190870 polymorphism near *LBX1* holds the potential as a predictive marker for AIS and among various genotypes, the T allele is highly associated with AIS susceptibility [1,2].

Although the role of rs11190870 near *LBX1* in the occurrence of AIS seemed well established, its association with AIS severity remains debatable. Previous studies suggested the association between rs11190870 near *LBX1* with curve progression in AIS, in which patients with TT and TC genotypes had a larger Cobb angle compared to those with CC genotypes [5,11,12]. However, a meta-analysis showed that SNP rs11190870 was not associated with the severity of the scoliosis curve in AIS [2]. Moreover, a replication study on a large number of patients in Japan found a marginal association between SNP rs11190870 and curve severity [13].

Despite the increasing body of evidence, most GWAS studies on AIS were conducted in East Asian populations [1,2,14]. To date, no study has characterized the genetic profile of AIS patients in the Southeast Asian population. Therefore, the aim of this study was to investigate the genetic profile of AIS patients in the Acehnese population in Indonesia, focusing on the *LBX1* SNP rs11190870. Furthermore, this study also aimed to confirm the association between rs11190870 near *LBX1* and the severity of AIS.

Methods

Study design and setting

A cross-sectional design was conducted on patients with AIS who visited the Orthopedic and Traumatology Department of Dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia. The study was conducted between July to December 2022. Clinical examination and blood sample collection were conducted at Dr. Zainoel Abidin General Hospital, while genetic examination was conducted at the Genetics Laboratory, Faculty of Veterinary Medicine, Universitas Syiah Kuala, Banda Aceh, and Prodia Laboratory, Jakarta, Indonesia.

The study protocol was reviewed and approved by the Institutional Health Research Ethics Committee and informed consent was obtained from the parents or legal guardians, along with assent from each participant before enrollment.

Study participants and variables

Female AIS patients of Acehnese ethnicity aged 10–18 years with Cobb angle >10 degrees who visited the Spine Division, Orthopedic and Traumatology Department, Dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia between 2021 and 2022 were invited to participate in this study. All of them underwent clinical examination by a spine surgeon, radiological examination, and genetic examination. Individuals with secondary scoliosis and neurological deficits were excluded from this study.

Demographic characteristics (age, ethnicity, residence) were recorded and preliminary clinical assessments (plumb line, scoliometer measurements, and Adam's test) were conducted. Radiological examinations were conducted at the Radiology Department and included posteroanterior (PA) and lateral standing spinal radiographs. These were used to measure Cobb angles to quantify curve severity, assess vertebral rotation using the Nash-Moe classification, identify the scoliosis apex, evaluate coronal balance using the Central Sacral Vertical Line (CSVL), determine skeletal maturity based on the Risser sign, and characterize the sagittal spinal profile (hypokyphotic, normokyphotic, or hyperkyphotic) based on thoracic Cobb angles. Genetic examination was conducted on all subjects to examine the rs11190870 near *LBX1* and its genotypes.

SNP genotyping

Genomic DNA was extracted from venous blood using Qiagen DNeasy Blood and Tissue Kit (Qiagen GmbH, Hilden, Germany). Genetic analyses focusing on the *LBX1* SNP rs11190870 were conducted at the Genetics Laboratory, Faculty of Veterinary Medicine, Universitas Syiah Kuala, and Prodia Laboratory, Jakarta, employing TaqMan SNP Genotyping Assays and Real-Time PCR (Bio-Rad, Hercules, California, USA) to determine allelic variants (TT, TC, CC).

Statistical analysis

Descriptive statistics (mean±SD, median with interquartile range, frequency, and percentage) were used to summarize demographic, clinical, and radiological variables. The potential role of rs11190870 in disease progression was assessed quantitatively with the Cobb angle. Cobb angle–measured through spinal X-ray–was classified into three categories: mild (10°–25°), moderate (25°–45°), and severe (>45°) [15]. The median score of the Cobb angle was used to analyze the association of *LBX1* SNP rs11190870 genotype and curve progression using an independent Student t-test or the Mann-Whitney U test, depending on the normality of the data. Statistical significance was set at $p<0.05$, and all statistical analyses were carried out using SPSS version 27 (IBM Corp., Armonk, NY, USA).

Results

In total, 30 female AIS patients of Aceh ethnicity participated in this study. The mean age was 15.8 years, with a mean Cobb angle of 26.49 degrees (**Table 1**). Most of the participants had right hump (70%), were categorized in C CSVL (63.3%), had Risser sign ≥4 (63.3%), and had normokyphotic thoracic sagittal profile (53.3%). Demographic and clinical characteristics of study participants are presented in (**Table 1**).

Table 1. Demographic and clinical characteristics of study participants

Characteristics	Frequency (percentage)
Age (year), mean±SD	15.8±1.84
Scoliometry, mean±SD	37.01±20.46
Plumb line test	
Right	21 (70.0)
Left	9 (30.0)
Cobb angle (degree), mean±SD	26.49±13.8
Mild (10°–25°); n (%)	5 (16.7)
Moderate (25°–45°)	22 (73.3)
Severe (>45°)	3 (10.0)
Central sacral vertical line (CSVL)	
A	6 (20.0)
B	10 (33.3)
C	14 (46.7)
Nash Moe, median (min-max)	1 (0–3)
Risser Sign, median (min-max)	4 (1–5)
Risser<4	11 (36.7)
Risser≥4	19 (63.3)
Thoracic sagittal profile	
Hypokyphotic	14 (46.7)
Normokyphotic	16 (53.3)

LBX1 SNP rs11190870 genotype study

Analysis of *LBX1* SNP rs11190870 revealed that the T allele was more prevalent (73.3%) than the C allele (26.7%) among AIS patients in the Acehnese population. A total of 16 individuals (53.3%) presented with a heterozygote TC genotype, while the other 14 (46.7%) presented with a homozygote TT genotype. No patients presented with the homozygote CC genotype in this study (**Table 2**).

Characteristics of study participants based on their genotypes are presented in (**Table 2**). Both TT and TC genotype groups shared similar traits in age (mean age was 15 in both groups), severity (most of the patients in both groups had moderate severity as measured with Cobb angle), and maturity of the curvature (most of the patients in both groups had Risser ≥4) (**Table 2**). The vast majority of patients in the TC group (81.3%) had a hump on the right side while those in the

TT group had an equal number of the right and left humps. Most of the patients in the TC group (75%) had thoracal apex, in contrast to the TT groups where most patients (57.1%) had lumbar apex. Patients with the TT genotype showed a bigger median score (8) than those with the TC genotype. No significant association was found between *LBX1* genotype and coronal balance (measured by central sacral vertical line (CVSL)), vertebral rotation (assessed using Nash Moe classification), skeletal maturity (measured with Risser sign), and sagittal profile (**Table 2**). However, a significant association was found between *LBX1* genotype and curve severity measured by Cobb angle (p=0.006). The characteristics of patients in both groups and their association with the *LBX1* genotype are presented in (**Table 2**).

Table 2. Characteristics of study participants based on their genotypes

Characteristics	*LBX1* rs11190870 genotype		*p*-value
	Homozygote TT (n=14)	Heterozygote TC (n=16)	
Age (year), mean±SD	15.18±1.35	15.68±2.15	0.801
Scoliometry, median (min-max)	8 (4.5–22)	5 (5–18)	0.190
Plumb line test			0.122
Right	7 (50.0)	17 (81.3)	
Left	7 (50.0)	3 (18.7)	
Cobb angle (degree)			0.006*
Mild (10°–25°)	0 (0.0)	5 (31.3)	
Moderate (25°–45°)	11 (78.6)	11 (68.8)	
Severe (>45°)	3 (21.4)	0 (0.0)	
Central sacral vertical line (CSVL)			0.291
A	3 (21.4)	3 (18.8)	
B	2 (14.3)	8 (50)	
C	9 (64.3)	5 (31.3)	
Nash Moe			0.124
Neutral	3 (21.4)	6 (37.5)	
Grade 1	3 (21.4)	4 (25)	
Grade 2	5 (35.7)	6 (37.5)	
Grade 3	3 (21.4)	0 (0.0)	
Risser sign			0.236
Risser <4	6 (42.9)	3 (18.8)	
Risser ≥4	8 (57.1)	13 (81.3)	
Thoracic sagittal profile			0.090
Hypokyphotic	11 (78.6)	16 (100.0)	
Normokyphotic	3 (21.4)	0 (0.0)	

*Statistically significant at p<0.05

Association of *LBX1* rs11190870 and curve progression

Further analysis was conducted to confirm the association between *LBX1* genotype and curve progression. This study found a significant difference between the median Cobb angle in patients with the TT and TC genotypes, 26 degrees and 22 degrees, respectively, p=0.01 **(Figure 1)**.

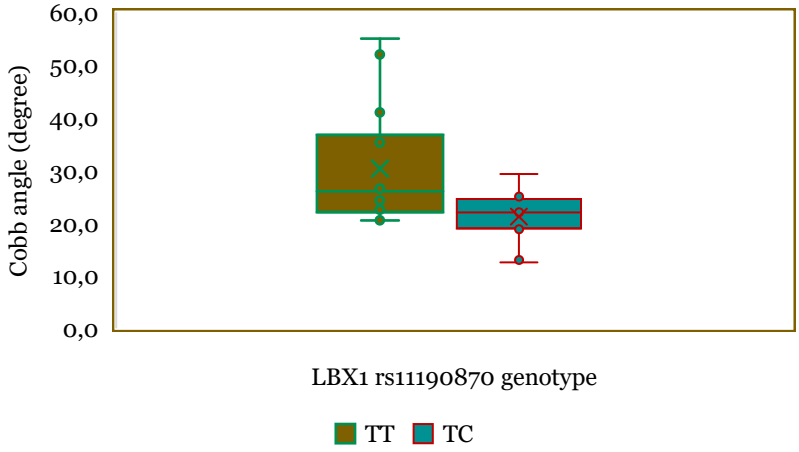

Figure 1. Comparison of median Cobb angle between the TT and TC genotypes.

Discussion

This study found that the majority of AIS patients in the Acehnese population had T alleles. Meta-analyses have consistently implicated the T allele at rs11190870 as a risk factor for AIS [1, 2], with individuals carrying the TT genotype having higher odds of developing AIS due to the presence of two risky T alleles [16,17]. Furthermore, a study in the Southeast European population also found that individuals with the TT genotype had a 35% higher risk of developing AIS than those with other genotypes [18]. However, some studies, such as Li *et al.* [19], did not find a significant effect on the TT genotype, indicating variability in genetic susceptibility across different ethnic groups. Given Aceh's complex ancestral background, including influences from Arab, Chinese, Indian, and European lineages [20], it is plausible that the *LBX1* variant distributions might mirror other diverse populations, resulting in different haplotypes and linkage disequilibrium (LD) patterns that affect AIS susceptibility.

Regarding patients' age, this study found that the mean age of AIS patients in the Acehnese population is 15 years old, regardless of the rs11190870 genotype. This finding aligns with studies from Scotland and Norway, which reported the most common onset of AIS in females at around 14 to 14.5±2.1 years of age [21]. Similarly, research conducted in Padang between 2013 and 2019 also identified female AIS patients with a mean age of 15.13 years, consistent with the global trend that AIS more commonly affects females [22]. Epidemiological evidence suggests that females have up to five-fold greater risk of curve progression than males, potentially due to hormonal influences, earlier growth spurts, postural factors, estrogen-receptor involvement, and differences in physical activity levels [23,24].

This study found no significant association between *LBX1* rs11190870 genotype and clinical characteristics such as age, coronal balance (measured by CVSL), vertebral rotation (assessed using Nash Moe classification), skeletal maturity (measured with Risser sign), and sagittal profile. Only curve severity was significantly associated with the *LBX1* rs11190870 genotype. However, it is important to highlight these clinical characteristics, particularly the skeletal maturity and curve severity. Most of the patients in this study (in both genotype groups) had moderate severity (Cobb angle 25°–45°) and Risser ≥4. These two parameters are important in deciding the management of AIS. According to the International Scientific Society on Scoliosis Orthopedic and Rehabilitation Treatment (SOSORT) guideline 2016, the treatment for AIS patients with moderate severity (Cobb angle 25°–45°) and Risser ≥4 includes physiotherapeutic scoliosis-specific exercises (PSSE) and full-time use of a rigid brace. Surgery is only indicated in AIS patients with Risser ≥4 and Cobb angle >45°[25]. Once the skeletal maturity is reached (Risser ≥4), progressivity of the curvature is likely to happen. Thus, conservative treatment with exercise and bracing should be adequate. However, low compliance with bracing and exercise might lead to severe AIS, which requires surgical intervention.

This study found a significant association between *LBX1* rs11190870 genotype and curve severity (p=0.01), in which AIS patients with the TT genotype had a larger Cobb angle than those with the TC or CC genotype. This is in line with a previous study in the Chinese population that suggested the effect of the T allele on curve progression [5]. This finding also confirms previous studies suggesting that the T allele is the risk allele that might be involved in both the initiation and progression of AIS [5,9,10]. The ability to distinguish individuals at high risk of curve progression is pivotal as it would facilitate early treatment, which is both effective for patients and economically beneficial for their families.

Several studies have been conducted to examine the association between the rs11190870 genotype and the severity of AIS (**Table 3**). This association was first investigated by Jiang *et al.* [5] in a Han Chinese population. This study found that AIS patients with the TT genotype had a significantly larger Cobb angle compared to individuals with the TC or CC genotype (p=0.005). Following this study, four studies (two on the Chinese population and two on the Japanese population) were conducted to further investigate this association. However, none of these studies found a significant association between rs11190870 and curve severity in AIS patients [11-14]. In the present study, we found that AIS patients with the TT genotype had significantly higher Cobb angles compared to those with the TC genotype. This finding raises further questions regarding the potential of *LBX1* rs11190870 in predicting AIS severity.

Table 3. Comparison of studies assessing the association between LBX1 rs11190870 and AIS severity

Study	Population	Number of AIS patients	Cobb angle of TT (mean±SD)	Cobb angle of TC (mean±SD)	*p*-value
Jiang *et al.*, 2013 [5]	Chinese	314	34.1±11.6	32.0±13.8	0.0005*
Gao *et al.*, 2013 [11]	Chinese	234	30.10±14.81	30.73±19.56	0.33
Takahashi *et al.*, 2015 [12]	Japanese	2,068	39.0±15.4	40.2±16.4	0.20
Takahashi *et al.*, 2018 [13]	Japanese	1,860	41.7±16.5	42.0±16.6	0.13
Man *et al.*, 2019 [14]	Chinese	176	47.2±15.3	47.4±19.4	0.679

*Statistically significant at $p<0.05$

Several theories have been proposed on how *LBX1* rs11190870 influences the severity of AIS. The SNP rs11190870 has been consistently associated with AIS susceptibility and severity across multiple populations. Studies in East Asian populations, including Chinese and Japanese cohorts, have shown that the T allele of rs11190870 is significantly associated with an increased risk of AIS and larger Cobb angles, indicating greater curve severity [5,13,14,26]. In a Han Chinese population, AIS patients with the TT genotype at rs11190870 had significantly larger Cobb angles compared to those with the TC or CC genotypes [5]. Similarly, a replication study in Japanese patients confirmed that rs11190870 was associated with curve severity, with the T allele correlating with more severe spinal curvature [13]. These findings suggest that rs11190870 influences the progression and severity of AIS.

The *LBX1* gene has been implicated in the pathogenesis of AIS through its role in regulating paraspinal muscle development and energy metabolism. A study showed that *LBX1* expression is asymmetric in the paraspinal muscles of AIS patients, with a higher expression on the convex side of the curvature compared to the concave side [27]. This asymmetry may contribute to the progression of spinal curvature by altering the balance of muscle growth and function around the spine. Furthermore, functional assays have demonstrated that silencing *LBX1* in myosatellite cells inhibits cell viability and myotube formation, highlighting the importance of *LBX1* in muscle development [28]. *LBX1* has also been linked to energy metabolism, where a loss of *LBX1* in skeletal muscle results in increased systemic energy expenditure and resistance to high-fat diet-induced obesity [29]. This suggests that *LBX1* may play a role in regulating metabolic pathways that influence the energy balance of paraspinal muscles, potentially contributing to the progression of scoliosis.

Animal models have provided valuable insights into the role of *LBX1* in AIS pathogenesis. In zebrafish, overexpression of *LBX1* or its homologs (*lbx1a, lbx1b,* and *lbx2*) caused body axis deformation through defects in convergent extension during embryonic development, contributing to the severity of AIS [30]. These defects were associated with downregulation of wnt5b, a ligand in the non-canonical Wnt/planar cell polarity (PCP) pathway, which is critical for proper tissue orientation and morphogenesis. Rescue experiments with wnt5b or RhoA, a downstream effector of Wnt/PCP signaling, attenuated the curvature phenotype, suggesting that *LBX1* overexpression disrupts Wnt/PCP signaling, leading to axial defects [30]. In mice, deletion of a conserved genomic region near *LBX1* resulted in vertebral rotation and proprioceptive deficits, phenotypes reminiscent of human AIS [31]. These findings underscore the importance of *LBX1* in maintaining proper spinal alignment and function.

Epigenetic modifications, such as DNA methylation, have been implicated in the regulation of *LBX1* expression in AIS. A study examining methylation levels of the *LBX1* promoter in deep paravertebral muscles found that patients with severe AIS (Cobb angle >70°) had higher methylation levels at specific CpG sites on the convex side of the curvature compared to those with less severe curves [32]. This suggests that epigenetic modifications may play a role in the localized regulation of *LBX1* expression, contributing to the progression and severity of scoliosis.

Haplotype analysis has revealed that rs11190870 and other SNPs near *LBX1* form distinct haplotypes with opposite effects on AIS risk. A recessive risk haplotype (TTA) was associated with increased susceptibility, while a co-dominant protective haplotype (CCG) reduced the risk of AIS [33]. These findings highlight the complexity of genetic regulation at the *LBX1* locus and the

potential for population-specific effects. Interestingly, the association of rs11190870 with AIS has not been universally replicated in all populations. A study in a South-Asian Indian population found no significant association between rs11190870 and AIS susceptibility, suggesting genetic heterogeneity in the etiology of AIS across different populations [34].

Based on the evidence from genetic, functional, and epigenetic studies, a proposed mechanism for the role of rs11190870 in AIS severity is as follows: (a) genetic predisposition, the rs11190870 SNP increases *LBX1* expression by enhancing the transcriptional activity of its promoter region [28,30]; (b) disruption of Wnt/PCP signaling, overexpression of *LBX1* disrupts Wnt/PCP signaling, leading to defects in convergent extension and axial elongation during embryonic development [30]; (c) asymmetric muscle development, elevated *LBX1* expression in paraspinal muscles on the convex side of the curvature contributes to asymmetric muscle growth and function, exacerbating spinal curvature [27]; and (d) epigenetic regulation: DNA methylation at the *LBX1* promoter region may locally regulate *LBX1* expression in paraspinal muscles, further contributing to the progression and severity of scoliosis [32]. The proposed mechanism for the role of rs11190870 in AIS severity is illustrated in (**Figure 2**). Key findings on the influence of *LBX1* rs11190870 and AIS are summarized in (**Table 4**).

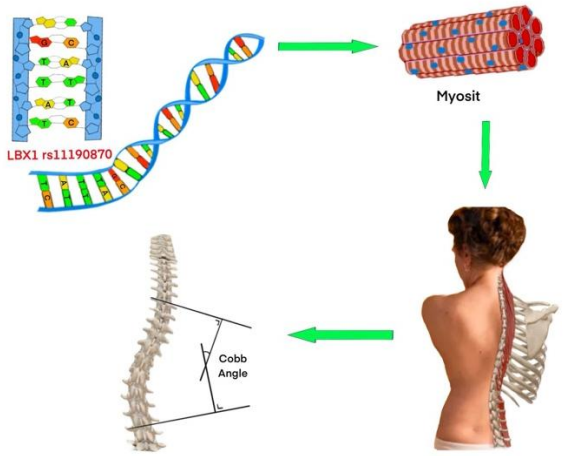

Figure 2. Presence of rs11190870 SNP (especially the T allele) alters the regulation of *LBX1* expression, resulting in impaired migration and differentiation of muscle precursor cells. Consequently, the development of paraspinal myocytes is disrupted, leading to an imbalance in paraspinal muscle function (between the convex and concave sides), which in turn causes postural abnormalities, specifically scoliosis.

Table 4. Summary of key findings on rs11190870 and *LBX1* in AIS

Study focus	Key findings	Studies
Genetic association	rs11190870 is associated with AIS susceptibility and severity in East Asian populations.	[5,13,14,26]
Functional role of *LBX1*	*LBX1* regulates paraspinal muscle development and energy metabolism.	[27-29]
Animal models	Overexpression of *LBX1* causes body axis deformation and disrupts Wnt/PCP signaling.	[30]
Epigenetic regulation	Methylation of *LBX1* promoter correlates with AIS severity	[32]
Population-specific effects	No association of rs11190870 with AIS in South-Asian Indian populations	[34]

This is the first study examining the genetic profile of the Indonesian population. However, its relatively small sample size should be considered when interpreting the results. Despite the growing prevalence of AIS in the Asian population, Indonesia lacks a screening program for AIS, resulting in a small number of patients visiting the study center. Another limitation is the case-only design, which limits further analysis of the association between *LBX1* rs11190870 and AIS in the Acehnese population. Nevertheless, as the first study conducted in Indonesia and Southeast Asia, this study serves as a crucial foundation for future research with a better design, larger

sample size, and more diverse ethnic representation to further investigate the role of *LBX1* rs11190870 in AIS.

Conclusion

This is the first study to examine the characteristics of genetic profiles and their association with curve progression in the Acehnese population. The findings of this study suggest that the rs11190870 polymorphism might serve as a predictor of AIS severity in the Acehnese population. This study also highlights the importance of scoliosis screening programs for school-aged children in Aceh since early detection can help prevent the progressivity of the curve and lead to more conservative treatment instead of surgical interventions. Further investigation through integrated genome-wide and epigenome-wide association studies to examine the role of *LBX1* rs11190870 in the susceptibility and severity of AIS in the Indonesian population is warranted.

Ethics approval

The study protocol was reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Syiah Kuala–RSUDZA Banda Aceh (Approval No. 410/EA/FK-RSUDZA/2021), and informed consent was obtained from the parents or legal guardians, along with assent from each adolescent participant before enrollment.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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References

1. Luo M, Zhang Y, Huang S, *et al*. The susceptibility and potential functions of the lbx1 gene in adolescent idiopathic scoliosis. Front Genet 2020; 11:614984.
2. Li YL, Gao SJ, Xu H, *et al*. The association of rs11190870 near LBX1 with the susceptibility and severity of AIS, a meta-analysis. Int J Surg 2018; 54(Pt A):193-200.
3. Li M, Nie Q, Liu J, *et al*. Prevalence of scoliosis in children and adolescents: A systematic review and meta-analysis. Front Pediatr 2024;12:1399049.

4. Komang-Agung IS, Dwi-Purnomo SB, Susilowati A. Prevalence rate of adolescent idiopathic scoliosis: Results of school-based screening in Surabaya, Indonesia. Malays Orthop J 2017;11(3):17-22
5. Jiang H, Qiu X, Dai J, *et al*. Association of rs11190870 near LBX1 with adolescent idiopathic scoliosis susceptibility in a Han Chinese population. Eur Spine J 2013; 22(2):282-286.
6. Cao Y, Min J, Zhang Q, *et al*. Associations of LBX1 gene and adolescent idiopathic scoliosis susceptibility: A meta-analysis based on 34,626 subjects. BMC Musculoskelet Disord 2016;17:309.
7. Khanshour AM, Wise CA. The genetic architecture of adolescent idiopathic scoliosis. in pathogenesis of idiopathic scoliosis. Tokyo: Springer Japan 2018.
8. Simony A, Carreon LY, Karen H, *et al*. Concordance rates of adolescent idiopathic scoliosis in a danish twin population. Spine 2016;41(19):1503-1507
9. Takahashi Y, Kou I, Takahashi A, *et al*. A genome-wide association study identifies common variants near LBX1 associated with adolescent idiopathic scoliosis. Nat Genet 2011; 43(12):1237-1240.
10. Fan YH, Song YQ, Chan D, *et al*. SNP rs11190870 near LBX1 is associated with adolescent idiopathic scoliosis in southern Chinese. J Hum Genet 2012; 57(4):244-246.
11. Gao W, Peng Y, Liang G, *et al*. Association between common variants near LBX1 and adolescent idiopathic scoliosis replicated in the Chinese Han population. PLoS One 2013; 8(1):e53234.
12. Takahashi Y, Inaba I, Kono K, *et al*. rs11190870 is not associated with severity of adolescent idiopathic scoliosis in Japanese. Scoliosis 2015; 10:1-2.
13. Takahashi Y, Kou I, Ogura Y, *et al*. A Replication Study for the Association of rs11190870 With Curve Severity in Adolescent Idiopathic Scoliosis in Japanese. Spine 2018; 43(10):688-692.
14. Man GC-W, Tang NL-S, Chan TF, *et al*. Replication study for the association of GWAS-associated loci with adolescent idiopathic scoliosis susceptibility and curve progression in a Chinese population. Spine 2019; 44(7):464-471.
15. Kikanloo SR, Tarpada SP, Cho W. Etiology of Adolescent Idiopathic Scoliosis: A Literature Review. Asian Spine J 2019; 13(3):519-526.
16. Erkkila IP, Reynolds CA, Weissman JP, *et al*. Factors associated with presentation of severe adolescent idiopathic scoliosis. J Pediatr Soc North Am 2023; 5(3):651.
17. Chen S, Zhao L, Roffey DM, *et al*. Association of rs11190870 near LBX1 with adolescent idiopathic scoliosis in East Asians: A systematic review and meta-analysis. Spine J 2014;14(12):2968-2975.
18. Nikolova S, Dikova M, Dikov D, *et al*. Positive association between a polymorphic locus near the LBX1 gene and predisposition of idiopathic scoliosis in Southeastern European population. J Appl Biomed 2019;17(3):184-189.
19. Li Y-L, Gao S-J, Xu H, *et al*. The association of rs11190870 near LBX1 with the susceptibility and severity of AIS, a meta-analysis. Int J Surg 2018;54:193-200.
20. Chalid I. Sejarah Aceh, Antara Damai dan Perang Memaknai Indonesia. Lhokseumawe, Universitas Malikussaleh 2014.
21. Souza Fld, Ferreira RBD, Labres D, *et al*. Epidemiology of adolescent idiopathic scoliosis in students of the public schools in Goiânia-GO. Acta Ortop Bras 2013;21(4):223-225.
22. Lee J-Y, Moon S-H, Kim HJ, *et al*. The prevalence of idiopathic scoliosis in eleven year-old Korean adolescents: A 3 year epidemiological study. Yonsei Med J 2014;55(3):773-778.
23. Dunn J, Henrikson NB, Morrison CC, *et al*. Screening for adolescent idiopathic scoliosis: evidence report and systematic review for the us preventive services task force. JAMA 2018;319(2):173-187.
24. Vialle R, Thévenin-Lemoine C, Mary P. Neuromuscular scoliosis. Orthop Traumatol Surg Res 2013;99:S124-S139
25. Negrini S, Donzelli S, Aulisa AG, *et al*. 2016 SOSORT guidelines: Orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth. Scoliosis Spinal Disord 2018;13:3.
26. Liang J, Xing D, Li Z, *et al*. Association between rs11190870 olymorphism Near LBX1 and susceptibility to adolescent idiopathic scoliosis in East Asian population: A genetic meta-analysis. Spine 2014; 39(11):862-869.
27. Kudo D, Miyakoshi N, Hongo M, *et al*. LBX1 mRNA expression in paravertebral muscles of patients with adolescent idiopathic scoliosis : A Preliminary Study. Spine Deform 2015;3(2):122-127.
28. Xu L, Feng Z, Dai Z, *et al*. A functional SNP in the promoter of LBX1 Is associated with the development of adolescent idiopathic scoliosis through involvement in the myogenesis of paraspinal muscles. Front Cell Dev Biol 2021;9:777890.
29. Nakagawa T, Horiuchi K, Kagami K, *et al*. The alteration of LBX1 expression is associated with changes in parameters related to energy metabolism in mice. Plos One 2024; 19(8):e0308445.

30. Guo L, Yamashita H, Kou I, *et al*. Functional investigation of a non-coding variant associated with adolescent idiopathic scoliosis in zebrafish: Elevated expression of the ladybird homeobox gene causes body axis deformation. PLoS Genet 2016;12(1):e1005802.
31. McCallum-Loudeac J, Moody E, Williams J, *et al*. Deletion of a conserved genomic region associated with adolescent idiopathic scoliosis leads to vertebral rotation in mice. Hum Mol Genet 2024;33(9):787-801.
32. Janusz P, Tokłowicz M, Andrusiewicz M, *et al*. Association of LBX1 gene methylation level with disease severity in patients with idiopathic scoliosis: Study on deep paravertebral muscles. Genes 2022;13(9):1556.
33. Chettier R, Nelson L, Ogilvie JW, *et al*. Haplotypes at LBX1 have distinct inheritance patterns with opposite effects in adolescent idiopathic scoliosis. PLoS One 2015;10(2):e0117708
34. Singh H, Shipra, Gupta M, *et al*. First report of evaluation of variant rs11190870 nearby LBX1 gene with adolescent idiopathic scoliosis susceptibility in a South-Asian Indian population. medRxiv 2022;28(6)22276987.