The Impact of Vitamin D on Adolescent Idiopathic Scoliosis

Siyi Wu

Shanghai No. 1 Experimental School Affiliated to SISU, Shanghai, China
Email: 5583404@qq.com

***Abstract*—In our modern society, there's growing attention to spinal health. China Children's Development Center reports a troubling 20% incidence of scoliosis in Chinese children and adolescents. This phenomenon also happened in other countries, which underscores the urgency of studying scoliosis in adolescents. This paper bases on previous research to investigate the vitamin D's influence on adolescent scoliosis, including the condition's basics, underlying mechanisms, and the latest research results. It primarily focuses on how vitamin D affects bone health, its role in Adolescent Idiopathic Scoliosis (AIS), and the causes of AIS. Through a comprehensive analysis of professional research literature, it becomes evident that vitamin D plays a vital role in scoliosis. Its primary mechanisms include enhancing bone density, supporting musculoskelet al health, and interacting with the vitamin D receptor, all pivotal for bone metabolism. Vitamin D is closely related to the central nervous system and brain development. It has an impact on the endocrine system, bone development, muscle growth, and central nervous system development, which are intricately linked to the origins of AIS. In conclusion, vitamin D shows promise for preventing and treating AIS. This study aims to provide insights into AIS of adolescent spinal healthcare, raise awareness of protecting Spinal health among adolescents and society, and ultimately improve human's health.**

***Keywords*—Adolescent Idiopathic Scoliosis (AIS), vitamin D, cause, mechanism, method**

I. Introduction

In recent years, the impact of spinal sub health on society has become increasingly evident, especially among younger individuals. As our society continues to advance, the focus on spinal health, both within our country and globally, is steadily growing.

The spine, composed of 33 vertebrae, is often referred to as the body's second lifeline. It is a crucial part of the human body, serving as the central axis for physical movements and the maintenance of our posture. Additionally, it plays a role in cushioning the body from shocks, providing protection to our internal organs.

According to statistics from the China Children's Development Center, the incidence of scoliosis among children and adolescents in China has reached a concerning 20%. Research from Beijing University of Chinese Medicine indicates that a significant portion of adults, around 80%, who experience symptoms like headaches, dizziness, blurred vision, lower back strain, limb discomfort, and numbness can trace these issues back to spinal abnormalities during their childhood and adolescence [1].

Some of the more common spinal conditions include lumbar spondylosis and cervical spondylosis. Patients suffering from these diseases mainly show symptoms such as headache, dizziness, elevated blood pressure and arrhythmia. In some cases, individuals may also experience nausea, vomiting, stomach pain, diarrhea, and sexual dysfunction [2]. Hence, it is imperative that we prioritize research into scoliosis during childhood and adolescence, as this issue cannot be overlooked.

During childhood and adolescence, scoliosis can manifest in various forms, including primary scoliosis, congenital scoliosis, neuromuscular scoliosis, and Adolescent Idiopathic Scoliosis (AIS). However, AIS is the most common type of scoliosis. There are several factors that may contribute to the development of AIS. These include factors such as height, gender, a family history of spinal diseases, inappropriate classroom chair height, incorrect standing posture, improper sitting posture, and a deficiency of vitamin D in the diet [3].

Vitamin D is a fat-soluble vitamin that belongs to a group of steroid-derived compounds with anti-rickets properties [4]. The two main forms are vitamin D3 and vitamin D2. Research suggests that a deficiency of vitamin D in the diet is a significant cause of AIS, with severe implications for the spinal health of adolescents. Researchers and society are currently focused on finding solutions to this issue in hopes of bringing relief to affected individuals.

With a foundation of previous research on the influence of vitamin D on adolescent scoliosis, this paper is based on these latest findings. It conducts an analytical study of the relevant aspects concerning the impact of vitamin D on scoliosis. This includes fundamental information about the condition, the underlying mechanisms, and the latest research findings. The primary focus of this study is on understanding the causes of AIS, exploring the effects of vitamin D on bone health, and assessing the influence of vitamin D on AIS.

Through this research analysis, the aim is to provide scoliosis patients with valuable insights for better treatment and contribute meaningful value to future

Manuscript received September 23, 2024; revised October 29, 2024; accepted December 6, 2024; published February 25, 2025.

medical research. Simultaneously, it seeks to raise awareness about spinal health issues, enabling those already affected by the condition to have a better understanding of their condition and encouraging those who have not been affected to take spinal health seriously, ultimately aiding in the prevention of scoliosis.

This proposal will analyze research content in distinct sections. Introduction begins with an overview of spinal function, common diseases, and introduces the topic of scoliosis. Discuss the scoliosis types, the influencing factors, and the impact of vitamin D on AIS. Emphasize the importance of exploring the role of vitamin D in spinal health and outline research objectives and methods. In the next section, we get know the structure of vitamin D and its functions, spinal physiology, scoliosis definition, and AIS clinical manifestations, and we also analyze AIS causes and the vitamin D-AIS relationship. Finally, we discuss our research in two aspects, the first one is to explore mechanisms of vitamin D in adolescent scoliosis, the second one is to discuss the harm of vitamin D deficiency in spinal health, and suggesting methods to cure this disease.

II. The Structure of Vitamin D and Scoliosis

A. The Structure and Functions of Vitamin D

1) The structure of vitamin D

Vitamin D is a fat-soluble vitamin, classified as a steroidal compound. It exhibits stable chemical properties, resisting heat and oxidation in neutral and alkaline solutions. However, in acidic solutions, it gradually decomposes. Various forms of vitamin D are known, with the most significant ones being vitamin D2 and D3 and their structure are shown in Fig. 1. Their structures are quite similar, differing mainly in their side chains.

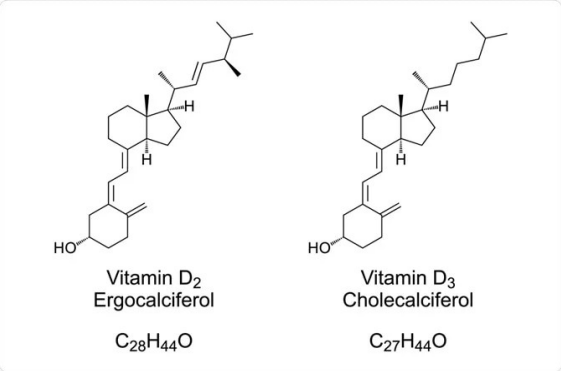

Fig. 1. The structure of vitamin D2 and D3 [5].

Vitamin D2, chemically known as ergocalciferol, is a steroidal compound formed through the photolytic cleavage of sterols and can be generated through the action of ultraviolet light on ergosterol.

Vitamin D3, also referred to as cholecalciferol, is produced from 7-dehydrocholesterol, which is derived from cholesterol after a process of dehydrogenation. It is formed upon exposure to ultraviolet light.

The specific form of vitamin D produced depends on the precursor compound, with ergosterol yielding vitamin D2 and 7-dehydrocholesterol leading to vitamin D3 [6].

2) Functions of vitamin D

Both types of vitamin D share the same physiological functions, enhancing calcium and phosphorus absorption and metabolism in organs such as the intestines, liver, and kidneys.

This supports the growth and differentiation of bone cells, ensuring overall bone health. Vitamin D is primarily produced by the body and obtained from animal-based foods [4].

Apart from its role in bone health, vitamin D has other functions. Population studies have shown a link between vitamin D deficiency and an increased risk of Type 2 Diabetes Mellitus (T2DM), with vitamin D deficiency as a potential risk factor for T2DM. Additionally, vitamin D deficiency is closely related to cardiovascular diseases. In the general population, low vitamin D levels are associated with conditions like coronary artery disease, heart attacks, heart failure, strokes, cardiovascular disease mortality, and overall mortality. Vitamin D deficiency is an independent risk factor for cardiovascular diseases [7].

B. Spinal Structure and Function

The human body is complex, with each part having a crucial role in maintaining normal function. The spine, often called the body's "second lifeline", is made up of 33 vertebrae (7 cervical, 12 thoracic, 5 lumbar, and 9 sacral and coccygeal vertebrae), with its structure shown in Fig. 2. These vertebrae are connected by ligaments, joints, and intervertebral discs. The spine runs vertically above the pelvis, supporting the shoulders, upper limbs, and head. It also acts as the posterior wall for the chest, abdominal cavity, and pelvic cavity, providing structural support and protecting internal organs. The spine has four natural curves (cervical lordosis, thoracic kyphosis, lumbar lordosis, and sacral kyphosis), giving it an "S"-shaped appearance when viewed from the side [1].

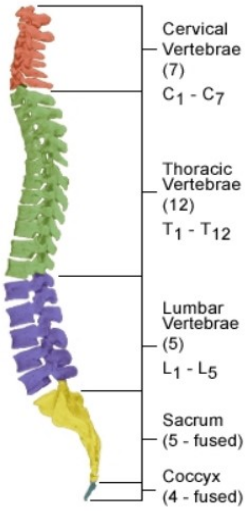

Fig. 2. The structure of spine [8].

Protected by the spine, the spinal cord is responsible for transmitting information, including movement and sensation. It works alongside spinal nerves to control the normal activities and operations of the body's internal organ systems. Additionally, the spine is closely linked to the circulatory system and indirectly influences internal organ functions through blood vessels [1].

Today, spinal diseases are affecting teenagers more frequently, with scoliosis being the most common issue. Therefore, addressing this problem through research is crucial.

C. Definition of Scoliosis

Scoliosis is a common musculoskelet al disorder affecting the spine, ribs, and the overall position of the trunk, caused by structural changes in the spine and surrounding tissues [9, 10]. The International Research Society on Scoliosis defines scoliosis as spinal curvature, measured using the Cobb method on an upright X-ray, with an angle greater than 10° [11], which is shown in Fig. 3. The most prevalent type of scoliosis is Adolescent Idiopathic Scoliosis (AIS), which often occurs for unknown reasons, with a significantly higher incidence during the critical growth and development period of adolescence, significantly impacting the physical and mental health of affected individuals.

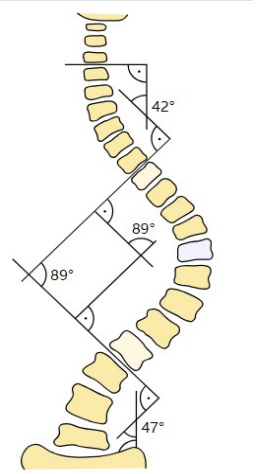

Fig. 3. The structure of scoliosis [12].

D. Clinical Presentation of AIS

AIS presents both physiological and psychological symptoms [13]. Physiologically, AIS typically involves lateral spine curvature and vertebral rotation. Clinical signs may include reduced height, uneven shoulders, uneven chest, spine deviation, waist skin creases, and, in severe cases, the development of a "razorback" deformity, whose characteristic is shown Fig. 4. This condition can affect lung development, leading to recurring respiratory issues and infections. Neurological symptoms may also occur [14]. Psychologically, AIS can negatively impact patients. Wang *et al.* [15] found that psychological factors and cultural background significantly affect scoliosis patients' adherence to brace treatment. The visible deformity can cause significant psychological distress, making it challenging for patients to accept their condition and the burdens of brace treatment. This can result in suboptimal treatment outcomes and contribute to depressive moods. Therefore, psychological factors are crucial in the treatment process. Huang [16] emphasized the importance of psychological care in promoting the recovery of adolescent scoliosis patients. Current treatment options for AIS include regular observation, Physiotherapeutic Scoliosis Specific Exercises (PSSE), bracing, and surgery [17], for patients with Cobb angles less than 45, it is recommended to adopt non-surgical treatment, as shown in Table I.

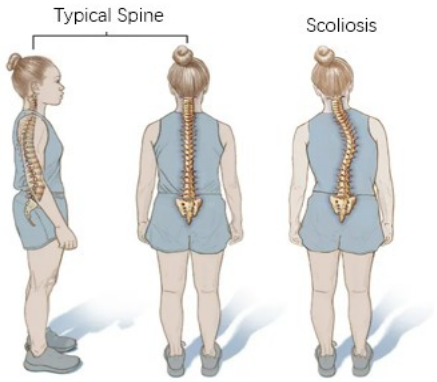

Fig. 4. The difference between typical spine and scoliosis [18].

TABLE I. THE TREATMENT OF AIS

Cobb angle	Treatment
10–20°	Regular observation, PSSE
20–45°	Regular observation, brace, PSSE
> 45°	Surgery

III. ANALYSIS OF THE MAIN CAUSES OF AIS

A. Major Factors in the Development of AIS

The exact cause of AIS is still uncertain. Research has explored multiple factors, but the complex nature of AIS makes it challenging to pinpoint a specific cause. Studies suggest that scoliosis may be influenced by factors like genetics, gender, hormones, and a lack of vitamin D in the diet [19, 20]. Key factors contributing to its development include genetics, gender, hormones, and dietary vitamin D deficiency.

1) The relationship between genes and AIS

AIS patients have significantly higher methylation level and lower PITX1 gene expression when compared to normal controls. In AIS patients, PITX1 methylation is significantly associated with the Cobb angles of main curves [21]. Rare gene variations in AIS have only sometimes been the subject of studies, and the field of study is quite new. Several genes, including FBN1, FBN2, HSPG2, POC5, and AKAP2, that may affect the occurrence and/or severity of scoliosis have been discovered through sequencing utilizing either whole exome or targeted gene panels [22].

2) Gender, hormones, and their relationship to AIS

AIS incidence shows significant gender differences, and this aligns with findings from various domestic and international studies. Among these, females constitute a high-risk group for developing scoliosis. Research emphasizes that during the pre-menarche adolescent phase, females exhibit a higher incidence of scoliosis compared to males. In cases with severe curvature (Cobb angle > 10°), the number of affected females is twice that of males, and for angles exceeding 30°, the ratio becomes eight times higher for females compared to males [23, 24]. Burwell *et al.* [25] proposed a pathogenic theory regarding scoliosis in females. This theory suggests that scoliosis in females may result from the lack of coordination in the development of the autonomic nervous and somatic nervous systems between the spine and the trunk. This lack of coordination may selectively increase the sensitivity of the hypothalamus to circulating leptin, leading to decreased leptin levels, affecting the sympathetic nervous system's axial regulation of skelet al growth, ultimately triggering scoliosis.

3) The connection between vitamin D and AIS

Moreover, research indicates that vitamin D deficiency in the diet is a crucial factor leading to AIS, as it can induce AIS by affecting the structure and function of the spine. Vitamin D plays an essential role in the body, including calcium homeostasis, immune regulation, and endocrine regulation. Higher levels of vitamin D have been linked to increased bone density, a lower fracture rate, and improved neuromuscular function [23, 26]. There is relevant evidence suggesting that the risk of suspected scoliosis symptoms in individuals with a dietary vitamin D deficiency and those unaware of their vitamin D status is 3.097 times and 2.121 times higher, respectively, compared to those with no vitamin D deficiency [3]. The following will elaborate on the significant impacts of vitamin D on scoliosis.

B. The impact of vitamin D on AIS

Current research on the pathogenesis of AIS suggests multiple mechanisms, primarily classified into four types: paraspinal muscle development, bone density, vitamin D receptors, and endocrine hormones. Vitamin D mainly plays an important role in maintaining bone and muscle growth, calcium homeostasis and regulating endocrine hormones (estrogen/leptin), which is closely related to the pathogenesis of AIS.

1) The effect of vitamin D on paraspinal muscles

Pathological changes in the paraspinal muscles in cases of scoliosis exhibit a consistent pattern: atrophied muscles on the convex side and muscle contractures on the concave side. Under electron microscopy, observations include a reduction in muscle fiber and mitochondrial content on the convex side, along with smaller mitochondria. Conversely, there is an increase in glycogen and fibroblast proliferation in the muscle tissue [27]. In patients with scoliosis, the distribution of type I and type II muscle fibers in the paraspinal muscles is imbalanced, in contrast to the relatively balanced distribution of these muscle fibers in the paraspinal muscles of normal individuals.

Experiments have demonstrated that severe vitamin D deficiency can lead to atrophy of type II skelet al muscle fibers. A deficiency in vitamin D results in an excessive production of Reactive Oxygen Species (ROS) in skelet al muscles, a reduction in mitochondrial oxidative phosphorylation, damage to mitochondrial function, and ultimately muscle fiber atrophy. This sequence of events contributes to the development of scoliosis, with a more pronounced vitamin D deficiency corresponding to more severe AIS symptoms [28].

2) The influence of vitamin D on bone density

Normal vitamin D levels are crucial for bone growth. Vitamin D deficiency can affect the deposition of bone minerals [29] and the differentiation of mesenchymal stem cells into osteoblasts, thereby impacting bone formation and reducing bone plasticity [30]. Bone is a structured organ that includes the bone marrow cavity and gaps within the bone structure. True bone density refers to the mineral content within a specific volume of bone tissue. However, since it is not feasible to measure individual structures separately, bone density is theoretically defined as the mineral content within a unit of tissue or organ [31]. This structure is shown in Fig. 5.

The process of acquiring bone mass occurs during the first stage of life and is expressed through balanced bone growth. An analysis of relevant studies found that there was no statistically significant association between vitamin D deficiency and bone mass development in children aged 6–9 years (P = 0.084). In contrast, in the 10–13 year age group, vitamin D deficiency increased the risk of inadequate bone mass development by 36% (PR=1.36, 95% CI=1.04-1.80). Moreover, in the 14–17 year age group, individuals with vitamin D deficiency had a 52% higher risk of inadequate bone mass development compared to those with sufficient vitamin D levels [32].

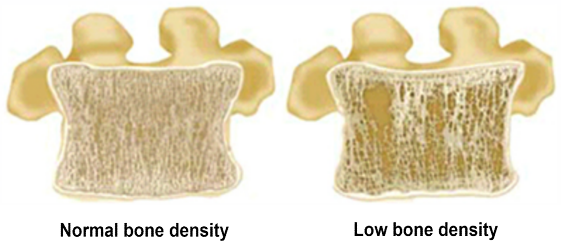

Fig. 5. The difference between normal/low bone density [33].

3) The role of vitamin D and its receptor genes

Vitamin D is a central regulatory factor in bone metabolism, and the Vitamin D Receptor (VDR) plays a crucial role in maintaining calcium and phosphorus metabolism. Bone metabolism is a complex process involving multiple factors [34, 35]. Xia *et al.* [36] conducted an analysis of VDR gene polymorphisms in Chinese female AIS patients and healthy adolescents to explore the relationship between VDR gene polymorphism and low bone mass and abnormal growth patterns in AIS patients. The results indicated that the primary function of the VDR gene is to regulate the stability and activity of VDR mRNA, which is closely related to adolescent bone density.

4) The effects of vitamin D levels on hormones

Research has shown that vitamin D deficiency can reduce the production of estrogen [37]. Insufficient estrogen levels lead to decreased bone density [38]. This further supports the evidence of abnormal bone growth and sustained reduction in bone density in AIS patients. There is also direct research confirming the relationship between decreased bone mass in AIS patients and vitamin D deficiency [39, 40]. Leptin levels are inversely related to 25-hydroxy vitamin D levels, with lower 25(OH)D levels associated with increased leptin levels [41].

IV. How Vitamin D Affects AIS

A. Mechanisms of How Vitamin D Affects AIS

Based on the above discussion, the impact mechanisms of vitamin D on AIS can be categorized into four aspects: (1) Vitamin D deficiency reduces estrogen production, (2) Vitamin D deficiency affects skelet al muscle generation, (3) Leptin levels are inversely related to 25 (OH) D levels, and (4) Vitamin D plays a role in brain development, and its association with central abnormalities in AIS patients is significant.

1) How vitamin D deficiency reduces estrogen levels

According to the research conducted by Chen *et al.* [42]. on vitamin D-deficient mouse models, it was found that vitamin D deficiency led to reduced gonadal function. Knocking out the Vitamin D Receptor (VDR) in female mice resulted in uterine atrophy and damaged follicles, with an increase in uterine weight upon estrogen supplementation. A significant decrease in serum 25 (OH) D levels, in line with a vitamin D deficiency model, accompanied the reduced estrogen levels. Estrogen is closely related to bone metabolism, participating in various ways to maintain the stability of the bone microenvironment. It is involved in the physiological processes of osteoblasts and osteoclasts, contributing to the dynamic balance of bone formation and bone resorption [43]. However, AIS is more prevalent in female patients, and estrogen plays a role in promoting osteoblast differentiation and maintaining normal bone density. Therefore, abnormalities in estrogen secretion may lead to impaired bone development and maturation. Among estrogens, E2 is the most biologically active and predominant component [44]. Research has indicated that Estrogen Receptor alpha (ERα) gene polymorphism is closely related to bone density, and Estrogen Receptor beta (ERβ) Alu I gene polymorphism is closely associated with the degree of AIS curvature [45].

Estrogen primarily affects AIS in two ways: first, it regulates osteoclasts, and second, it modulates osteoblasts. According to Oursler *et al.* [46], Estrogen Receptors (ER) are present in osteoclasts, and specific knockouts of ERα in osteoclasts can result in trabecular bone loss. Estrogen also extends the lifespan of osteoblasts and inhibits apoptosis, mainly through ER-mediated rapid activation of kinases. Studies have found the presence of ER in osteoblast precursor cells and osteoblasts, suggesting that estrogen has a direct influence on the bone formation process and exerts an indirect effect independent of ER [43].

Currently, there are two main viewpoints regarding the impact of estrogen on AIS:

1. Abnormal estrogen levels cause delayed menarche in females, leading to delayed bone development and maturation, which increases the likelihood of spinal deformities.

2. Abnormal estrogen levels directly affect bone metabolism and bone remodeling, resulting in abnormal bone growth and development, thereby increasing the likelihood of AIS occurrence [11].

2) How vitamin D deficiency affects muscle growth

Research indicates that vitamin D deficiency can lead to muscle atrophy, proximal muscle weakness, and diffuse muscle pain. Researchers have detected the expression of the Vitamin D Receptor (VDR) and 1α-hydroxylase (CYP27B1) genes and proteins in human skelet al muscles, which has raised concerns about the potential for severe vitamin D deficiency to cause atrophy of type II skelet al muscle fibers. In a cell experiment exploring the effects of 1α, 25-(OH)2D on C2C12 myoblast cell proliferation and differentiation, researchers intervened with 1α, 25-(OH)2D (100 nM) in C2C12 myoblast cells. The experiment demonstrated that vitamin D promotes VDR expression and myoblast differentiation capacity. Vitamin D inhibits the expression of the muscle growth inhibitory factor, myostatin [47]. 1α, 25-(OH)2D promotes myoblast cells to differentiate into myotubes, significantly increasing the expression of myotube differentiation markers such as myogenin (MYOG) and troponin T type 1 (TNNT) genes [28, 48]. In AIS patients, there is a significant difference in the distribution of muscle fiber types between the concave and convex sides. The proportion of type I muscle fibers in the muscles on the convex side is higher, with deeper muscles being more prominent [49].

3) How vitamin D affects leptin levels

Leptin is a hormone closely associated with body composition. Leptin receptors in the hypothalamus bind to leptin, leading to signal transduction through the activation of Janus tyrosine protein kinases, affecting the secretion of various neuroendocrine hormones [50]. 25-hydroxy vitamin D is the active metabolite of vitamin D and is the most active form of the vitamin. Numerous studies have reported its role in regulating the differentiation of pig or mouse fat cells, with consistent findings. In recent years, research has also suggested that vitamin D's anti-tumor effects include inhibiting cancer cell proliferation and inducing apoptosis. According to Payet *et al.* [51], 1,25-dihydroxyvitamin D inhibits the proliferation and differentiation of 3T3-L1 preadipocytes. Leptin is primarily expressed in the cytoplasm and forms brownish granules around the nucleus. Different concentrations of 1,25-dihydroxyvitamin D have inhibitory effects on the expression of leptin in differentiating fat cells, suggesting that providing an appropriate amount of vitamin D may help control body weight and improve the secretion of lipogenic hormones in children [52].

AIS patients exhibit muscle dysfunction and asymmetry in paraspinal muscles [53]. Leptin increases muscle mass by inhibiting muscle fiber protein degradation and enhancing muscle cell proliferation [54]. Muscle mass and skelet al muscle mass is closely related to muscle strength [55]. Therefore, it is evident that leptin levels are closely related to AIS [23, 56].

4) How vitamin D impacts brain function

Vitamin D plays a crucial role in the central nervous system research related to AIS. The close association between scoliosis and syringomyelia, asymmetry in the brainstem of some AIS patients, and the presence of cerebellar tonsillar herniation in AIS have been observed [57]. Additionally, there is research indicating a potential link between the severity of scoliosis in girls and increased sensory integration impairments [58]. In patients with a Cobb angle greater than 15°, particularly in cases with sensory fusion, there is evidence of impaired central information processing, indicating central functional abnormalities [59]. Moreover, vitamin D has a role in human brain development, which may have an association with central abnormalities in AIS patients [23, 60].

There is evidence that vitamin D can be locally synthesized and metabolized in the central nervous system. An earlier study reported three major metabolites, 25-$(OH)D_3$, 1,25-$(OH)_2D_3$, and 24,25-$(OH)_2D_3$, present in human cerebrospinal fluid [61]. Furthermore, key enzymes involved in the breakdown metabolism of 25-$(OH)D_3$ have been discovered in brain cells, indicating that vitamin D plays a role in the differentiation of dopaminergic neurons and influences dopamine synthesis pathways by altering the expression of key enzymes. This can affect cholinergic, dopaminergic, and noradrenergic neurotransmitter systems [62].

Moreover, vitamin D deficiency has been associated with various neurological disorders such as amyotrophic lateral sclerosis [63], depression [64], and schizophrenia [65]. This suggests that vitamin D can regulate brain development, potentially benefiting the spinal health of adolescents and reducing the occurrence of AIS [66].

In summary, vitamin D deficiency or insufficiency is closely related to AIS, with its occurrence influenced by the regulation of muscle fibers, endocrine hormones, and bone mineral density. Vitamin D has various mechanisms by which it affects AIS, with the most significant impact on bones and muscles. Vitamin D can indirectly influence bone and muscle development through endocrine hormones, leading to the onset and progression of AIS.

Directly, vitamin D has a more substantial impact on bones and skelet al muscles, as some AIS patients experience bone loss, and 25-hydroxyvitamin D_3 [25-$(OH)_2$-VitD_3] is positively correlated with bone mineral density in normal individuals, which can lead to atrophy of type II muscle fibers. A randomized controlled trial by Lam *et al.* [67] assessed the role of vitamin D in improving bone health and controlling AIS progression, and the study showed that daily supplementation with 400/800 IU of vitamin D can improve bone mass in AIS patients and prevent curve progression. Vitamin D, under the action of the ligand 1,25-dihydroxyvitamin D3, binds to VDR and regulates the proliferation and osteogenic differentiation of Bone Marrow Mesenchymal Stem Cells (BMSC). BMSCs are multi-potent stem cells present in the bone marrow cavity, capable of differentiating into osteoblasts, chondrocytes, and adipocytes, and are central participants in bone metabolism. Many researchers speculate that unexplained spinal deformities and bone loss in AIS patients may be related to impaired BMSC function. The observed phenomenon is that AIS patients have impaired osteogenic differentiation ability of BMSCs, reduced calcium salt deposition ability, and decreased bone formation ability [68]. These two factors may be direct causes of AIS onset.

In conclusion, AIS patients experience a significant reduction in bone mass compared to age-matched healthy individuals, and Bone Mineral Density (BMD) is inversely correlated with the severity of scoliosis. This decrease in bone mass continues until the end of adolescence, impacting peak bone mass and potentially leading to complications such as osteoporosis in later life [69]. Although there are various indirect mechanisms influencing AIS, many unknown factors still require further research. As for treatment, there is currently no specific medication available, but some clinical studies have suggested that vitamin D supplementation has a positive effect on improving bone health. The main content overview of influence of lack vitamin D is shown in Fig. 6.

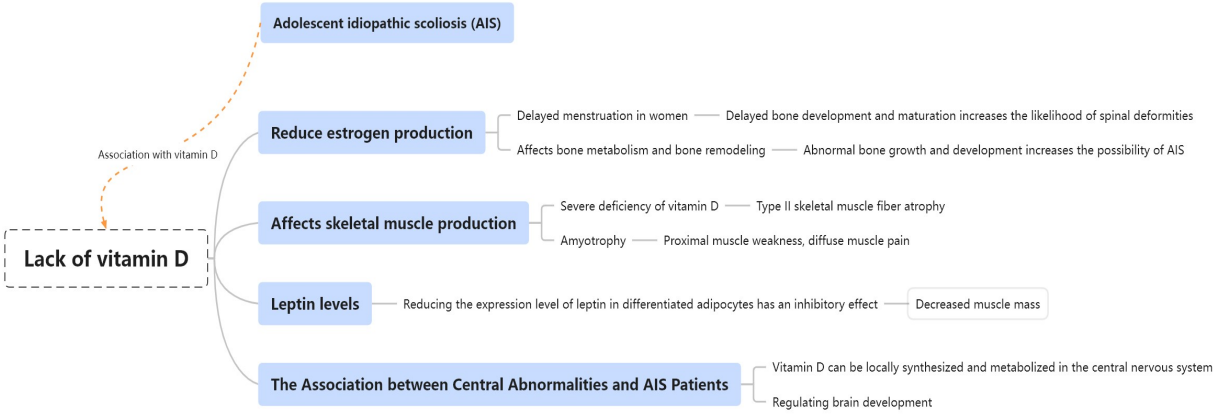

Fig. 6. The main content overview of influence of lack vitamin D.

B. *Strategies to Address the Impact of Vitamin D Deficiency on Adolescent Spinal Health*

1) Nutritional status of vitamin D in adolescents

It is estimated that there are 1 billion people worldwide suffering from a deficiency in vitamin D (25(OH)D < 50 nmol/l). Results from 14 studies conducted in various countries show that the prevalence of vitamin D deficiency in children and adolescents ranges from 19% to 91%. The nutritional status of vitamin D in Chinese children and adolescents is also a cause for concern. According to the National Nutrition and Health Survey conducted in 2010–2012, the detection rate of vitamin D deficiency in children and adolescents aged 6 to 17 was 53.20%. Research in Guangzhou, China revealed that the prevalence of vitamin D deficiency among children and adolescents aged 0 to 17 was 13.70% in 2009–2011 and 11.37% in 2015, with an increase in deficiency observed with age [32]. The lack of vitamin D is highly likely to lead to AIS, and supplementing vitamin D has a positive role in preventing or alleviating AIS. Through analysis and exploration, the following are the main solutions currently discussed in research.

2) Basic methods of vitamin D supplementation for adolescents

Sun exposure is the best way to synthesize vitamin D. In the subcutaneous tissues of the human body, there is a substance called 7-dehydrocholesterol which, when exposed to ultraviolet rays in sunlight, can be converted into vitamin D. Medically, 7-dehydrocholesterol is referred to as a vitamin D precursor or provitamin D. This form of vitamin D accounts for most of the body's vitamin D supply and is often referred to as the "sunshine vitamin" [70].

Diet is also a way for the body to obtain vitamin D, although it only accounts for a small portion of the total required vitamin D. Consequently, it can be challenging to obtain sufficient vitamin D through diet alone. In nature, foods rich in vitamin D are primarily certain types of marine fish. Since vitamin D is a fat-soluble vitamin, it is found in very small amounts in plant-based foods, with mushrooms being one of the few exceptions, containing around 100 IU of vitamin D per 100g of fresh mushrooms. Consuming milk is also a method of vitamin D supplementation, with approximately 100 IU of vitamin D in 240 mL of milk.

Taking preparations containing vitamin D can increase muscle strength, promote bone mineralization, improve balance, and thus reduce the risk of falls and related bone fractures [71].

Given that most children and adolescents in China have busy academic schedules and seldom have outdoor activities, considering supplementation with vitamin D is worthwhile. Options for supplementation include alfacalcidol medications and calcitriol capsules, which are typically rapidly converted into vitamin D3 and 25-hydroxyvitamin D3 in the liver. The latter is a metabolite of vitamin D3 and plays a crucial role in regulating calcium and phosphate metabolism.

In terms of supplement options, there are three choices: vitamin D, alfacalcidol, and calcitriol. Vitamin D2 and D3 are considered inactive forms, and they cannot be directly interconverted. Both are collectively referred to as vitamin D and must be converted into the active vitamin D form through metabolic processes in the liver and kidneys to exert their physiological effects. Alfacalcidol and calcitriol are active metabolites of vitamin D. Alfacalcidol undergoes rapid hydroxylation in the liver to become calcitriol, which promotes calcium and phosphate absorption in the intestines, increases serum calcium levels, and suppresses Parathyroid Hormone (PTH) secretion to reduce bone calcium dissolution.

Calcitriol is one of the most important metabolically active products of vitamin D3 in the human body. It can be rapidly converted into the most potent metabolite of vitamin D3, 1,25-dihydroxyvitamin D, which plays a crucial role in treating conditions such as rickets, hypoparathyroidism, and nutritional osteomalacia in patients dependent on dialysis. Calcitriol does not require specific liver or kidney function for activation, and its effects are typically faster but shorter-lasting compared to other vitamin D supplements. Additionally, it is the major active metabolite of vitamin D3 in the body, and therefore, there is usually no need to combine it with other vitamin D preparations after ingestion to avoid the risk of vitamin D toxicity [72].

In general, for adolescents, all three forms have vitamin D supplementation effects, which are dose and duration dependent. Adolescents can choose the most economical and convenient method based on their individual needs. Sun exposure is relatively simple, efficient, and has mood-regulating benefits. Dietary methods are practical and can be easily incorporated into daily life by adding foods rich in vitamin D. The third method, supplementing with vitamin D preparations, is highly efficient but may have certain side effects. Under normal conditions, this is not recommended. It is suggested that adolescents try various effective methods of vitamin D supplementation to find the one that suits them best, ultimately achieving the goal of actively preventing AIS. The overview of the major method about supplementing vitamin D is shown Fig. 7.

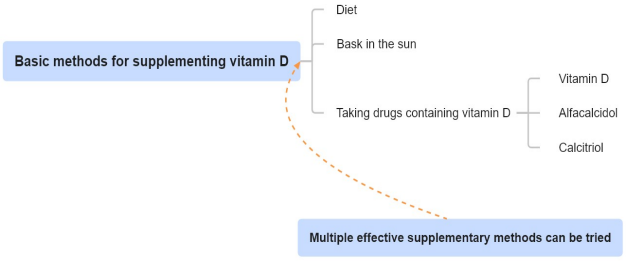

Fig. 7. The overview of the major method about supplementing vitamin D.

V. Conclusion

Research analysis indicates that as society develops and people's lifestyles change, the incidence of AIS is

increasing, and its impact is becoming more serious. AIS has multiple causes, and vitamin D deficiency is an important factor triggering AIS. This paper primarily conducts research and analysis through a literature review method, focusing on the impact of vitamin D on AIS, including its mechanisms, potential risks, and solutions.

The research analysis demonstrates that vitamin D has a significant influence on the development of scoliosis. It directly or indirectly affects the condition of scoliosis through the development of paraspinal muscles, bone density, vitamin D receptors, and endocrine hormones. Its main impact is on enhancing bone density and musculature, making it an essential component of bone metabolism. Vitamin D and vitamin D receptors are crucial factors in AIS. Moreover, vitamin D can be locally synthesized and metabolized in the central nervous system, relating to brain development. In addition, vitamin D affects the endocrine system, bone development, muscle growth, and central nervous system development, all of which are closely related to the mechanisms of AIS. Although there are numerous mechanisms by which vitamin D affects AIS, it has the most significant impact on the skelet al and muscular development of adolescent spines. Vitamin D can influence Bone Marrow Mesenchymal Stem Cell (BMSC) proliferation and osteogenic differentiation, which can lead to the onset and exacerbation of AIS.

While specific treatments for AIS are yet to emerge, clinical research has already suggested that supplementing vitamin D plays a role in prevention and treatment of AIS. We propose the primary methods of vitamin D supplementation, including exposuring to ultraviolet rays in sunlight, adjusting dietary sources, and ingesting vitamin D supplements. As part of a healthy lifestyle, exposure to sunlight and dietary sources are preferable means of supplementation. Although vitamin D deficiency is recognized as a critical factor in the AIS process, gaining a comprehensive understanding of its effects and mechanisms is important for understanding AIS's pathogenesis. Further research in this area, especially into its mechanisms, requires more extensive experimental evidence to substantiate the theoretical methods. This paper will be of reference value for the treatment and research of vitamin D in AIS, to raise awareness about AIS, and actively establish social protection mechanisms for AIS in our society.

CONFLICT OF INTEREST

The author has claimed that no conflict of interest exists.

REFERENCES

[1] L. F. Lou, "Anatomy and health management of spinal movement," *Health Vocational Education*, no. 15, pp. 158–159, 2018.

[2] S. C. Wang, "The necessity of regular spinal examinations and consultations for middle-aged women," *Chinese and Foreign Women's Health Research*, no. 19, pp. 84–85, 2019.

[3] P. R. Tian and X. Q. Ren, "Detection rate of suspected symptoms of adolescent scoliosis and logistic regression analysis of related factors," *Journal of Jilin Medical College*, no. 1, pp. 30–33, 2016. doi:10.13845/j.cnki.issn1673-2995.2016.01.011

[4] C. H. Yang, "Introduction to vitamin D," *Practical Medicine of China*, no. 3, pp. 243–244, 2009.

[5] L. J. Thomas. (2023). Vitamin D biochemistry. [Online]. Available: https://www.news-medical.net/health/Vitamin-D Biochemistry.aspx

[6] C. Carlberg, M. Raczyk, and N. Zawrotna, "Vitamin D: A master example of nutrigenomics," *Redox Biology*, vol. 62, 102695, 2023. https://doi.org/10.1016/j.redox.2023.102695

[7] J. M. Liu, J. M. Hou, and M. Zhu, "Extra-skelet al effects of vitamin D," *Chinese Journal of Osteoporosis and Mineral Diseases*, no. 1, pp. 61–68, 2018.

[8] Wikipedia. (2023). Vertebral column. [Online]. Available: https://en.wikipedia.org/wiki/Vertebral_column

[9] Y. G. Wang. (2023). Effects of adolescent scoliosis on lung function and lung development: An animal experimental study. Doctoral dissertation. Lanzhou University. [Online]. Available: https://kns.cnki.net/kcms2/article/abstract?v=xzY5Ip_Thcl-osKj0BngN2qC-x_ndVEIIrcVi2uPSlcqhFszy_M2mUoRm9-FuEBqb1AGsMAHLCU4wkoVJFVMViadhADyu8vQ1syLPzlfvJ5H4q2Ayq4E1JP4zhxWq1FT&uniplatform=NZKPT&language=CHS

[10] J. R. Kamerlink, I. Engel, *et al.*, "The treatment of vertebral and chest wall deformities with expandable thoracoplasty and a prosthetic expandable implant," *Journal of Pediatric Orthopedics*, vol. 30, no. 1, pp. 90–98, 2010.

[11] B. L. Cui, W. Fang, *et al.*, "Progress in the etiology of adolescent idiopathic scoliosis," *Medical Theory and Practice*, no. 18, pp. 3085–3087, 2022.

[12] Wikipedia. (2023). Scoliosis. [Online]. Available: https://en.wikipedia.org/wiki/Scoliosis

[13] M. Leal-Hernández, F. Martínez-Monje, *et al.*, "Analysis of the quality of life in patients affected by scoliosis," *Semergen*, vol. 44, no. 4, pp. 227–233, 2018. (In Spanish)

[14] P. C. Hsu, C. K. Feng, *et al.*, "Health-related quality of life in children and adolescent with different types of scoliosis: A cross-sectional study," *Journal of the Chinese Medical Association: JCMA*, vol. 82. no. 2, pp. 161–165, 2019.

[15] J. Wang, Z. Luo, L. H. Chen, and S. J. Yu, "Correlation analysis of aesthetic expectations, psychological and social factors, and compliance with corrective treatment in scoliosis patients," *Chinese Journal of Aesthetic Medicine*, no. 8, pp. 159–162, 2021.

[16] F. M. Huang, "Psychological nursing strategies for adolescent scoliosis patients," *Famous Doctor*, no. 3, p. 168, 2019.

[17] P. J. Gill, T. Thavam, *et al.*, "Identifying conditions with high prevalence, cost, and variation in cost in US children's hospitals," *JAMA Netw. Open*, vol. 4, no. 7, e2117816, 2021.

[18] Mayo Clinic. Scoliosis. [Online]. Available: https://www.mayoclinic.org/diseases-conditions/scoliosis/symptoms-causes/syc-20350716

[19] C. He and L. Li, "Study on the symmetry of surface electromyographic signals of paraspinal muscles in adolescents with idiopathic scoliosis and their correlation with the degree of curvature," *Biomedical Engineering and Clinical Medicine*, no. 2, pp. 150–155, 2022.

[20] Y. Peng, S. R. Wang, *et al.*, "Research progress on the etiology and pathogenesis of adolescent idiopathic scoliosis," *Chinese Medical Journal*, vol. 133, no. 4, pp. 483–493, 2020.

[21] D. Nada, C. Julien, *et al.*, "Identification of FAT3 as a new candidate gene for adolescent idiopathic scoliosis," *Scientific Reports*, vol. 12, no. 1, 12298, 2022.

[22] B. Shi, L. Xu, *et al.*, "Abnormal PITX1 gene methylation in adolescent idiopathic scoliosis: A pilot study," *BMC Musculoskelet al Disorders*, vol. 19, no. 1, p. 138, 2018.

[23] C. L. Wang and S. L. Wu, "Advances in the application of endocrine hormones in adolescent idiopathic scoliosis," *Chinese School Health*, no. 8, pp. 1276–1280, 2023.

[24] S. L. Weinstein, L. A. Dolan, J. C. Cheng, A. Danielsson, and J. A. Morcuende, "Adolescent idiopathic scoliosis," *Lancet (London, England)*, vol. 371, no. 9623, pp. 1527–1537, 2008.

[25] R. G. Burwell and R. K. Aujla, "Pathogenesis of adolescent idiopathic scoliosis in girls – A double neuro-osseous theory involving disharmony between two nervous systems, somatic and autonomic expressed in the spine and trunk: possible dependency

on sympathetic nervous system and hormones with implications for medical therapy," *Scoliosis*, vol. 4, no. 24, 2009.
[26] C. M. Patton, A. P. Powell, and A. A. Patel, "Vitamin D in orthopaedics," *The Journal of the American Academy of Orthopaedic Surgeons*, vol. 20, no. 3, pp. 123–129, 2012.
[27] X. Miao, "Characteristics of scoliosis in artistic gymnasts and changes in paraspinal muscle function," doctoral dissertation, Beijing Sport University, 2013.
[28] J. Zhang, J. Q. Lu, and R. F. Shi, "Role of vitamin D and its receptor in bone and muscle function," *Acta Nutrimenta Sinica*, no. 5, 2021.
[29] J. Y. Lee, T. Y. So, and J. Thackray, "A review on vitamin d deficiency treatment in pediatric patients," *The Journal of Pediatric Pharmacology and Therapeutics: JPPT: The Official Journal of PPAG*, vol. 18, no. 4, pp. 277–291, 2013.
[30] C. L. Wen, X. M. Fu, *et al.*, "Serum vitamin D levels in patients with idiopathic scoliosis and their clinical significance," *Modern Medicine*, no. 1, pp. 57–59, 2018.
[31] Q. W. Zheng. (2023). Study on the relationship between children's serum 25-hydroxyvitamin D and bone density. Master's thesis. Hebei Medical University. [Online]. Available: https://kns.cnki.net/kcms2/article/abstract?v=xzY5Ip_Thcn6XSHFcrrHbevh8fVqSfhyi9z91vHc__eX_dHtygO7Y6MJTQQqIC4DPm0rhQDIhfUV-rV-gE4-wS9V8pMeBdDmYXdWeH-_3_nXhAH8VMYLNemdQWQYFcpX3MDjvJLIVnM=&uniplatform=NZKPT&language=CHS
[32] L. P. Ao, "Effects of vitamin D metabolism-related genetic variations on vitamin D nutrition and bone mass development in children and adolescents," master's thesis, Guangdong Pharmaceutical University, 2021.
[33] River Radiology. (2016). Bone densitometry. [Online]. Available: https://www.riverradiology.com/services/bone-densitometry
[34] B. L. Riggs, T. V. Nguyen, *et al.*, "The contribution of vitamin D receptor gene alleles to the determination of bone mineral density in normal and osteoporotic women," *Journal of Bone and Mineral Research: The Official Journal of the American Society for Bone and Mineral Research*, vol. 10, no. 6, pp. 991–996, 1995.
[35] L. W. Sun, X. Q. Huang, and J. Huang, "Role of vitamin D and its receptor in bone metabolism in adolescents and its impact on patients with adolescent idiopathic scoliosis," *Chinese Journal of Spine and Spinal Cord*, no. 11, pp. 1041–1044, 2017.
[36] C. W. Xia, Y. Qiu, *et al.*, "Study on vitamin D receptor gene polymorphism in female patients with adolescent idiopathic scoliosis," *Chinese Medical Journal*, no. 21, pp. 1465–1469, 2007.
[37] K. Kinuta, H. Tanaka, *et al.*, "Vitamin D is an important factor in estrogen biosynthesis of both female and male gonads," *Endocrinology*, vol. 141, no. 4, pp. 1317–1324, 2000.
[38] A. Goździalska, J. Jaśkiewicz, *et al.*, "Association of calcium and phosphate balance, vitamin D, PTH, and calcitonin in patients with adolescent idiopathic scoliosis," *Spine*, vol. 41, no. 8, pp. 693–697, 2016.
[39] M. B. Balioglu, C. Aydin, *et al.*, "Vitamin-D measurement in patients with adolescent idiopathic scoliosis," *Journal of Pediatric Orthopedics, Part B*, vol. 26, no. 1, pp. 48–52, 2017.
[40] R. T. E. Silva, R. J. R. Fernandes, *et al.*, "Role of different hormones in the pathogenesis and severity of adolescent idiopathic scoliosis," *Acta Ortop Bras*, *Acta Ortopedica Brasileira*, vol. 25, no. 1, pp. 15–17, 2017.
[41] J. H. Kim and J. H. Choi, "Pathophysiology and clinical characteristics of hypothalamic obesity in children and adolescents," *Annals of Pediatric Endocrinology & Metabolism*, vol. 18, no. 4, pp. 161–167, 2013.
[42] Y. Z. Chen, Z. Qin, *et al.*, "Changes in sex hormones in mice with vitamin D deficiency," *Journal of Guizhou College of Traditional Chinese Medicine*, no. 3, pp. 8–9, 2012.
[43] D. Liu. (2020). Clinical study on the influence of premature No. 1 formula on bone metabolism in central precocious girls. Master's thesis. Nanjing University of Chinese Medicine. [Online]. Available: https://kns.cnki.net/kcms2/article/abstract?v=xzY5Ip_Thcn-mhkOZFdb3ZEjXSxTVjFmmhTqpfyHGFtDCXQVqq5k3Oa_IS7MnKg8BgJlyDPaKPTE4B67gCdESo-a5mOmXYWsyp82owOyi-tmtCG184oDo1c3wNgsYDogTt7CMzbolw8=&uniplatform=NZKPT&language=CHS
[44] T. I. Aksenovich, I. R. Semenov, E. K. Ginzburg, and A. M. Zaĭdman, "Preliminary analysis of inheritance of scoliosis," *Genetika*, vol. 24, no. 11, pp. 2056–2063, 1988.
[45] G. M. Lu. (2019). Study on the relationship between children's scoliosis and the expression of bone formation factors in blood. Master's thesis. Chongqing Medical University. (2019). [Online]. Available: https://kns.cnki.net/kcms2/article/abstract?v=xzY5Ip_ThckxV4ktJj4He5u698mOBLKLgT5zRe3T1dchPaiDh7ldV1da1m5A5IzYTHHOs4CuYdTfWoOlcptSrAo7Qtw2yrSuI-R36vjpUNqLyLjdFApQj3lAaYT0p9fNoOzvqqhDtsA=&uniplatform=NZKPT&language=CHS
[46] M. J. Oursler, P. Osdoby, *et al.*, "Avian osteoclasts as estrogen target cells," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 88, no. 15, pp. 6613–6617, 1991.
[47] L. A. Garcia, K. K. King, *et al.*, "1,25(OH)2vitamin D3 stimulates myogenic differentiation by inhibiting cell proliferation and modulating the expression of promyogenic growth factors and myostatin in C2C12 skelet al muscle cells," *Endocrinology*, vol. 152, no. 8, pp. 2976–2986, 2011.
[48] K. R. Montenegro, R. Carlessi, V. Cruzat, and P. Newsholme, "Effects of vitamin D on primary human skelet al muscle cell proliferation, differentiation, protein synthesis and bioenergetics," *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 193, 105423, 2019.
[49] X. H. Yin and L. Liang, "Histological observation of the muscles on both sides of patients with idiopathic scoliosis," *Journal of Clinical Anatomy*, no. 4, pp. 214–217, 1987.
[50] H. F. Yu and J. Gao, "Influence of vitamin D on the expression of adiponectin and leptin in human adipocytes," *China Medical Guide*, no. 11, pp. 72–73, 2013.
[51] T. Payet, M. Valmori, *et al.*, "Vitamin D modulates lipid composition of adipocyte-derived extracellular vesicles under inflammatory conditions," *Molecular Nutrition & Food Research*, vol. 67, no. 22, 2023.
[52] J. Gao. (2014). Effects of vitamin D on proliferation, differentiation of human adipocytes, and adipogenic hormones in obese children. Doctoral dissertation. Tianjin Medical University. [Online]. Available: https://kns.cnki.net/kcms2/article/abstract?v=xzY5Ip_ThckfiQh7S2VuUscOZYjjYEFF9xRpZWru20aTOwmvcVWdT7O-woyFUMIZZIwWI1nU29QmXYAhn9cmgKOQ7VIeCoERex87zJc4bGXqSytTzhNLgHF2Uhfe5qH8&uniplatform=NZKPT&language=CHS
[53] G. Zoabli, P. A. Mathieu, and C. E. Aubin, "Back muscles biometry in adolescent idiopathic scoliosis," *The Spine Journal: Official Journal of the North American Spine Society*, vol. 7, no. 3, pp. 338–344, 2007.
[54] N. Sáinz, A. Rodríguez, *et al.*, "Leptin administration favors muscle mass accretion by decreasing FoxO3a and increasing PGC-1alpha in ob/ob mice," *PloS One*, vol. 4, no. 9, e6808, 2009.
[55] E. M. S. Tam, Z. Liu, *et al.*, "Lower muscle mass and body fat in adolescent idiopathic scoliosis are associated with abnormal leptin bioavailability," *Spine*, vol. 41, no. 11, pp. 940–946, 2016.
[56] Y. Qiu, X. Sun, *et al.*, "Decreased circulating leptin level and its association with body and bone mass in girls with adolescent idiopathic scoliosis," *Spine*, vol. 32, no. 24, pp. 2703–2710, 2007.
[57] S. Y. Ng, J. Bettany-Saltikov, *et al.*, "The role of vitamin D in the pathogenesis of adolescent idiopathic scoliosis," *Asian Spine Journal*, vol. 12, no. 6, pp. 1127–1145, 2018.
[58] M. Beaulieu, C. Toulotte, *et al.*, "Postural imbalance in non-treated adolescent idiopathic scoliosis at different periods of progression," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 18, no. 1, pp. 38–44, 2009.
[59] T. Haumont, G. C. Gauchard, P. Lascombes, and P. P. Perrin, "Postural instability in early-stage idiopathic scoliosis in adolescent girls," *Spine*, vol. 36, no. 13, E847–E854, 2011.
[60] X. Cui, H. Gooch, A. Petty, J. J. McGrath, and D. Eyles, "Vitamin D and the brain: Genomic and non-genomic actions," *Molecular and Cellular Endocrinology*, no. 453, pp. 131–143, 2017.
[61] S. Balabanova, H. P. Richter, G. Antoniadis, *et al.*, "25-hydroxyvitamin D, 24, 25-dihydroxyvitamin D and 1,25-

dihydroxyvitamin D in human cerebrospinal fluid," *Klinische Wochenschrift*, vol. 62, no. 22, pp. 1086–1090, 1984.
[62] Y. Qin and S. F. Yang, "Research progress on the relationship between vitamin D and brain development," *Chinese Journal of Child Health*, no. 4, pp. 393–396, 2021.
[63] A. Langer-Gould, R. M. Lucas, A. H. Xiang, *et al.*, "Vitamin D-binding protein polymorphisms, 25-hydroxyvitamin D, sunshine and multiple sclerosis," *Nutrients*, vol. 10, no. 2, p. 184, 2018.
[64] M. J. Berridge, "Vitamin D and depression: Cellular and regulatory mechanisms," *Pharmacological Reviews*, vol. 69, no. 2, pp. 80–92, 2017.
[65] G. Valipour, P. Saneei, and A. Esmaillzadeh, "Serum vitamin D levels in relation to schizophrenia: A systematic review and meta-analysis of observational studies," *The Journal of Clinical Endocrinology and Metabolism*, vol. 99, no. 10, pp. 3863–3872, 2014.
[66] L. W. Chen and X. Cheng, "Research progress on the role of vitamin D in the nervous system," *Journal of Pediatric Pharmacy*, no. 2, pp. 59–62, 2021.
[67] T. P. Lam, V. W. Hung, H. Y. Yeung, *et al.*, "Quantitative ultrasound for predicting curve progression in adolescent idiopathic scoliosis: A prospective cohort study of 294 cases followed-up beyond skelet al maturity," *Ultrasound in Medicine & Biology*, vol. 39, no. 3, pp. 381–387, 2013.
[68] W. W. Park, K. T. Suh, J. I. Kim, S. J. Kim, and J. S. Lee, "Decreased osteogenic differentiation of mesenchymal stem cells and reduced bone mineral density in patients with adolescent idiopathic scoliosis," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 18, no. 12, pp. 1920–1926, 2009.
[69] Z. Zhang, J. J. Chen, Y. C. Meng, and X. H. Zhou, "Research progress on bone loss in adolescent idiopathic scoliosis," *Practical Orthopedics Journal*, no. 10, pp. 897–901, 2020.
[70] Q. Luo, "Sunshine vitamin – Vitamin D," *Family Medicine*, vol. 38, no. 11, November 2017.
[71] C. Y. Zhang, P. D. Bian, Z. X. Shou, and S. F. Qian, "The current status of vitamin D deficiency in the elderly and strategies," *China New Drugs and Clinical Journal*, no. 6, pp. 328–332, 2019.
[72] Baidu. What is the difference between alpha calcitriol and calcitriol? [Online]. Available: https://m.baidu.com/bh/m/detail/ar_17252816007924854921