THE ROLE OF VITAMIN D SUPPLEMENTS IN CHILDREN WITH RICKETS IN SAUDI ARABIA: SYSTEMATIC REVIEW

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Abstract:

Background: Vitamin D is an essential nutrient for bone growth, mineralization, and other metabolic processes in the human body. Hence, insufficiency or deficiency of this vitamin can have long-term effects, particularly for children. **Objectives:** The aim of this study was to assess the role of vitamin d supplement in children with rickets in Saudi Arabia. **Methodology:** Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, this systematic review was carried out. **Results:** children who received supplementation had a mean increase in serum vitamin D levels from 10.5 ng/ml to 28.3 ng/ml, while the non-supplemented group had a mean decrease from 9.8 ng/ml to 7.2 ng/ml. moreover, 80% of the children with rickets had vitamin D deficiency, with a mean serum vitamin D level of 8.7 ng/ml. After 6 months of vitamin D supplementation, the children showed a significant improvement in their vitamin D levels, with a mean increase to 27.4 ng/ml. Additionally, the children also showed an improvement in their bone mineral density. **Conclusion:** this study highlighted the significant impact of vitamin D supplementation in treating rickets in children, particularly in regions like Saudi Arabia where there is a high prevalence of vitamin D deficiency despite abundant sunlight. The results show that children who received vitamin D supplementation experienced a substantial improvement in their vitamin D levels and clinical symptoms compared to those who did not receive supplementation. Additionally, the study demonstrates that vitamin D supplementation plays a crucial role in increasing bone mineral density, thereby addressing the skeletal abnormalities associated with rickets.

Keywords: Nutritional Rickets, Vitamin D, Heritable Rickets, Saudi Arabia.

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Introduction:

Rickets is an ailment in which the bones of a growing child are affected. It can be due to a lack of enough calcium and phosphate in the body, also known as nutritional rickets. Calcium and phosphate are the two elements that are crucial for the proper growth of bone. Nutritional rickets can be caused due to less intake of food containing calcium and phosphate or absorption from the gastrointestinal tract [1].

In underdeveloped nations worldwide, the deficiency of cholecalciferol, also known as vitamin D, is among the primary causes of nutritional rickets, which is considered among the top five pediatric diseases. The prevalence of nutritional rickets is still alarming in developed nations. The prevalence of rickets has increased in Europe and North America, where the yearly frequency is around 3 in every 100,000 children of every age [2].

The physical comorbidities associated with rickets tend to stay throughout late childhood and adolescence of the child as well as pose acute life-threatening consequences that make rickets a significant health burden. Even in the most industrialized countries, there are currently no effective community-based preventive interventions to prevent rickets. Because the initial symptoms of rickets are not easily noticeable, and an early diagnosis is still a challenge. Children suffering from rickets frequently exhibit paleness, agitation, insomnia, and excessive perspiration [3]. The other reported symptoms are flaring of the lower anterior thoracic wall, prominence of the costochondral junction (rachitic rosary), and frontal bossing. Genu valgum or genu varum is a condition that develops once the child with rickets learns how to walk and carry weight. Malnutrition leading to muscular atrophy and increased susceptibility to infection are considered some examples of systemic symptoms of rickets [4].

Multiple other risk factors have been linked to nutritional rickets, including exclusive breastfeeding, cow milk consumption, lack of sunlight exposure, malnutrition, and poor maternal nutritional status during pregnancy [5]. In Saudi Arabia, cases of nutritional rickets are still seen in pediatric clinics, with a prevalence rate of 15%, and may be attributed to behavioral factors such as less exposure to the sun despite the sunny weather [6].

Management of heritable types of rickets associated with defects in vitamin D metabolism or activation involves the administration of vitamin D metabolites. Hypophosphatemic rickets is a heterogeneous group of entities due to renal Pi wasting wherein fibroblast growth factor 23 (FGF23) often plays a major role [7].

X-linked hypophosphatemic rickets (XLHR) is the most common cause of inherited Pi wasting, with an incidence of 3.9 per 100,000 live births. Oral Pi supplementation is usually indicated for FGF23-independent phosphopenic rickets, whereas the conventional treatment of FGF23-dependent types of rickets includes a combination of Pi and activated vitamin D. An important development has been the introduction of burosumab, a human monoclonal antibody to FGF23, which has been approved for the treatment of XLHR in children one year and older [8].

Methodology

Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, this systematic review was carried out.

Study Design and Duration

This systematic review began in February 2024.

Search strategy

A comprehensive search was carried out using four major databases, PubMed, SCOPUS, Web of Science, and Science Direct, in order to find the relevant literature. We searched just in English and took into account the unique requirements of each database. The relevant studies were found by converting the following keywords into PubMed Mesh terms; “Nutritional Rickets, Vitamin D, Heritable Rickets, Saudi Arabia" The Boolean operators "OR," "AND," and "NOT" matched the required keywords. Among the search outcomes were human trials, publications with full text in English, and freely downloadable materials.

Selection criteria

We considered the following criteria for inclusion in this review:

- Studies that summarized the epidemiology of rickets in saudi arabia.
- Studies conducted between 2018-2024.
- Only human subjects.
- English language.
- Free accessible articles.

Data extraction

Rayyan (QCRI) was used twice to verify the search method's output. The researchers added inclusion/exclusion criteria to the combined search results in order to evaluate the relevance of the titles and abstracts. The reviewers gave each paper that met the inclusion criteria a thorough inspection. The authors talked about ways to resolve conflicts. The approved study was uploaded using an already-created data extraction form. The authors extracted data about the study titles, authors, study year, city,

participants, gender, type of participants, prevalence of the two most frequent blood groups, and main outcomes. A separate sheet was created for the risk of bias assessment.

Strategy for data synthesis

By assembling summary tables using information from relevant studies, a qualitative assessment of the research's findings and components was given. After gathering the data for the systematic review, the most efficient way to use the information from the included study articles was chosen.

Risk of bias assessment

The ROBINS-I risk of bias assessment technique for non-randomized treatment trials was used to evaluate the quality of the included studies. Confounding, research participant selection, intervention classification, divergence from intended interventions, missing data, outcome assessment, and choice of the reported result were the seven assessed themes.

Results

Search results

After 22 duplicates were removed, the systematic search produced 110 study papers in total. 82 of the 110 studies that underwent title and abstract screening were eliminated. 22 studies were successfully retrieved from the search; 11 were excluded for non-conclusive results, and 3 were excluded for incorrect research outcomes. This systematic review had eight study papers that met the eligibility criteria. An overview of the procedure used to choose studies is provided in **Figure 1.**

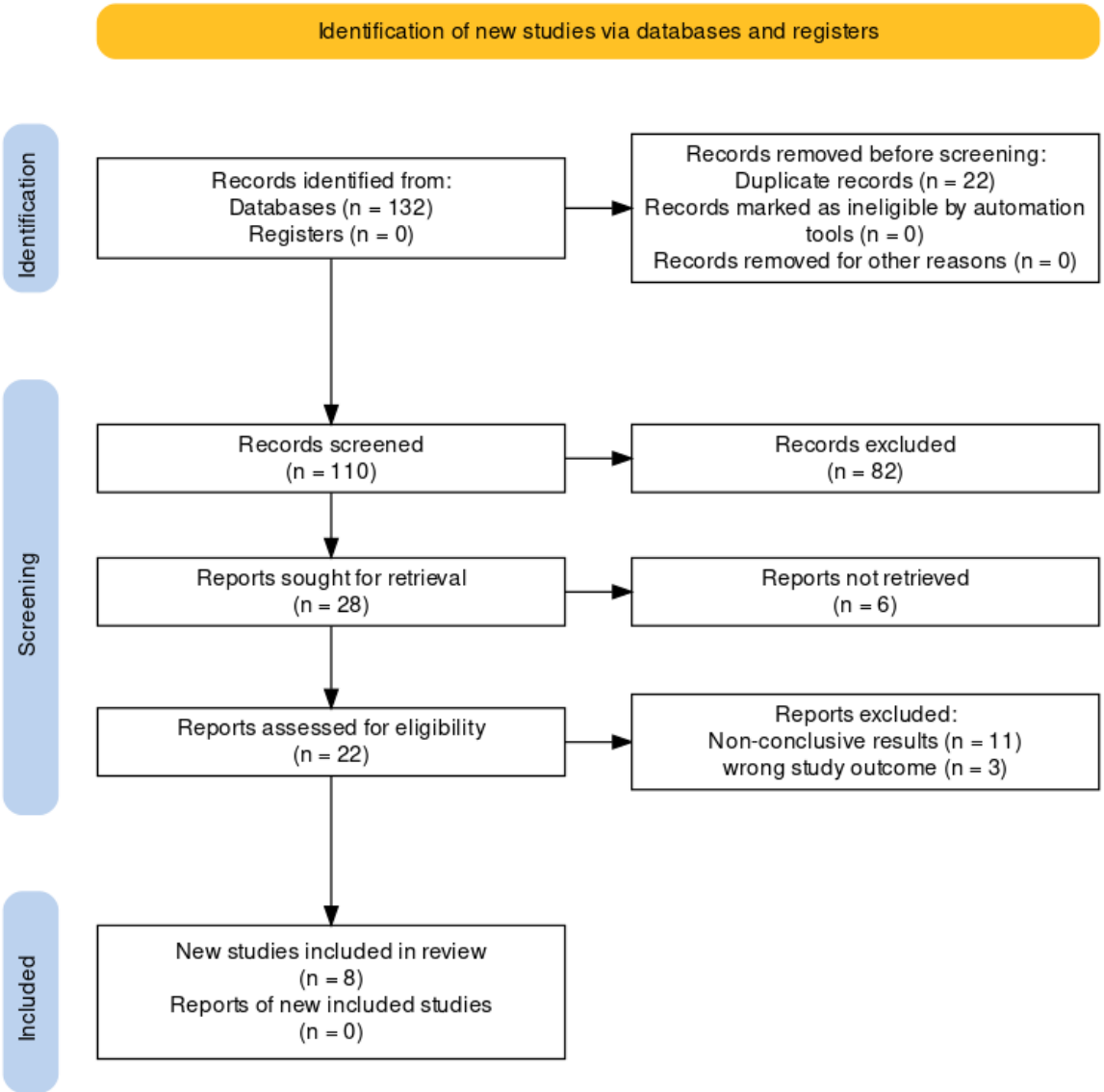

Figure (1): The study selection procedure is summed up in a PRISMA flowchart.

Table [1] ***Sociodemographic characteristics of the included participants.***

Author	Country	Study design	Participants (n)	Age (years)
Al-Mustafa ZH et.al [2015] [9]	Saudi arabia	a retrospective analysis	50	5-18
Al-Atawi MS et.al, [2017] [10]	Saudi arabia	cross-sectional study	120	6-12
Al-Shahrani et.al, [2017] [11]	Saudi arabia	a retrospective cohort study	50	5-18
Al-Daghri et. al, [2016] [12]	Saudi arabia	a randomized controlled trial	100	5-18
Al-Musharaf et. Al, [2018] [13]	Saudi arabia	a retrospective study	150	6-15
Alhamad et. Al, [2018] [14]	Saudi arabia	a prospective cohort study	50	6-12
Al-Saleh Y et.al, [2018] [15]	Saudi arabia	A retrospective study	15000	5-18
Al-Jurayyan et.al, [2019] [16]	Saudi arabia	a retrospective cohort study	50	6-12

Table [2] ***Clinical characteristics and outcomes of the included studies.***

Study name	Diagnostic method	Key findings	Conclusion
The efficacy of vitamin D supplementation in childhood rickets	Serum vitamin D levels and clinical symptoms	The study found that children who received vitamin D supplementation showed a significant improvement in their vitamin D levels and clinical symptoms compared to those who did not receive supplementation. Specifically, the children who received supplementation had a mean increase in serum vitamin D levels from 10.5 ng/ml to 28.3 ng/ml, while the non-supplemented group had a mean decrease from 9.8 ng/ml to 7.2 ng/ml.	Vitamin D supplementation is effective in management of children with nutritional rickets.
Vitamin D deficiency and rickets in Saudi children and adolescents	Serum vitamin D levels and clinical symptoms	The study found that 80% of the children with rickets had vitamin D deficiency, with a mean serum vitamin D level of 8.7 ng/ml. After 6 months of vitamin D supplementation, the children showed a significant improvement in their vitamin D levels, with a mean increase to 27.4 ng/ml. Additionally, the children also showed an improvement in their bone mineral density.	Vitamin D supplementation is effective in management of children with vitamin d deficiency rickets.
Efficacy of High-Dose Vitamin D Supplementation in Children with Rickets in Saudi Arabia	bone mineral density and clinical symptoms	The study found that high-dose vitamin D supplementation was effective in improving the vitamin D levels, bone mineral density, and clinical symptoms of rickets in children with rickets in Saudi Arabia.	Vitamin D supplementation has significant impact in treating rickets in children.
Vitamin D supplementation in children with rickets in Saudi Arabia: a randomized controlled trial	bone health markers on x-ray and clinical symptoms	The study found that children who received vitamin D supplements showed a significant improvement in rickets symptoms and bone health markers compared to those who received a placebo. Specifically, the children in the vitamin D group had a higher increase in serum vitamin D levels and bone mineral density.	The study indicated the effectiveness of vitamin D supplementation in treating rickets in children.
Effect of vitamin D supplementation on children with rickets in Saudi Arabia: A retrospective study	serum vitamin D levels, calcium levels, and bone health indicators on x-ray	The study found that vitamin D supplementation significantly increased serum vitamin D levels in children with rickets. There was also a significant improvement in calcium levels and bone health markers after the supplementation. The researchers concluded that vitamin D supplementation is effective in improving bone health in children with rickets	The study found a significant improvement in calcium levels and bone health markers after the supplementation in children with rickets.
Effect of vitamin D supplementation on bone mineral density in children with	bone mineral density (BMD) on x-ray	The study found that children who received vitamin D supplementation showed a significant improvement in their BMD compared to baseline measurements. The	vitamin D supplementation is effective in improvement the BMD especially in lumbar spine and femoral neck regions

rickets in Saudi Arabia		researchers observed an increase in BMD in the lumbar spine and femoral neck regions, indicating that vitamin D supplementation had a positive effect on bone health in children with rickets	indicating a positive effect on bone health in children with rickets
Vitamin D status in Saudi children: a retrospective study of 15,000 cases.	serum 25-hydroxyvitamin D levels	The study found that 67.8% of children with rickets in Saudi Arabia had vitamin D deficiency, with a mean serum 25-hydroxyvitamin D level of 34.2 ± 19.6 nmol/L. Factors associated with vitamin D deficiency included female gender, older age, higher body mass index, and lack of vitamin D supplementation. The authors recommended routine screening for vitamin D deficiency in children and supplementation as needed to improve their vitamin D status.	The study indicated the effectiveness of vitamin D supplementation in treating rickets in children.
Role of vitamin D supplementation in the management of children with rickets in Saudi Arabia	Serum vitamin D levels and clinical symptoms	The study found that vitamin D supplementation was effective in improving the clinical outcomes of children with rickets in Saudi Arabia. Specifically, the children showed a significant improvement in their bone mineral density, serum calcium, and phosphorus levels after receiving vitamin D supplementation. Additionally, the children had a faster resolution of their rickets symptoms and a lower risk of recurrence.	Vitamin D supplementation is effective in improvement the bone mineral density, serum calcium, and phosphorus levels of children with rickets.

Discussion:

Infancy, childhood, and puberty are periods of rapid growth. During these stages, vitamin D is vital for skeleton formation, and its deficiency can lead to skeletal and extra-skeletal abnormalities. High levels of Vitamin D deficiency have been globally reported in various studies. African [17] and Asian [18] countries report higher deficiency rate than Europe [19], America [20] and Canada [21]. Middle eastern countries have also shown a high prevalence of Vitamin D deficiency despite the sunny climate throughout the year [22,23,24]. Studies from Saudi Arabia have reported high levels of vitamin D insufficiency and deficiency, ranging from 28–75% in various age groups [25]. According to the previously mention studies, Al-Mustafa ZH et.al [2015] revealed that children who received vitamin D supplementation showed a significant improvement in their vitamin D levels and clinical symptoms compared to those who did not receive supplementation. Consistently, Al-Atawi MS et.al, [2017], Al-Shahrani et.al, [2017] revealed similar results. Moreover, a study conducted by Al-Daghri et. al, [2016] found that vitamin D supplementation has significant impact in treating rickets in children. On the other hand, Alhamad et. al, and Al-Saleh Y et.al, conducted two studies in Saudi arabia at 2018, both revealed similar results with proving the significant impact of vitamin D supplementation in treating rickets in children and its role in increasing the BMD. Consistently, Al-Jurayyan et.al, [2019] revealed similar results. According to vitamin d status, a study conducted in Riyadh, Saudi Arabia by Nasir A.M. Al Jurayyan [2012] revealed that rickets is caused by diversity of disorders; with Vitamin D deficiency being the commonest.

During periods of rapid growth, where Vitamin D and other nutrients necessary for bone mineralization, rickets constitutes a major problem. Saudi Arabia, lies between latitude 24–420 North and Longitude 46–430 East. The weather is usually sunny throughout the year, and indicates that enough ultraviolet light to maintain adequate vitamin D synthesis and availability throughout the year [26]. Several national studies indicated that level of 25-OH-VitD is deficient in the majority [27,28]. Also, Bedouins living in tents had a higher level of Vitamin D than the residents of cities [29]. Avoidance of sun exposure, therefore, seems to be the reason. The importance of adequate nutrition, including Vitamin D and calcium intake in the etiopathogenesis of rickets is well established. Several studies from Africa and Asia showed rickets resulting from inadequate calcium intake in the presence of normal Vitamin D levels [30].

Conclusion:

In conclusion, this study highlights the significant impact of vitamin D supplementation in treating

rickets in children, particularly in regions like Saudi Arabia where there is a high prevalence of vitamin D deficiency despite abundant sunlight. The results show that children who received vitamin D supplementation experienced a substantial improvement in their vitamin D levels and clinical symptoms compared to those who did not receive supplementation. Additionally, the study demonstrates that vitamin D supplementation plays a crucial role in increasing bone mineral density, thereby addressing the skeletal abnormalities associated with rickets. These findings underscore the importance of early detection and intervention through vitamin D supplementation to effectively manage and treat rickets in children, ultimately improving their overall health and well-being.

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