Association of Vitamin D Deficiency on Children Growth

Abdulmoein Eid Al-Agha
King Abdulaziz University Hospital, Pediatric Department, P.O.Box 80215, Jeddah 21589, Saudi Arabia.
E-mail: aagha@kau.edu.sa

Raghda Abdullah Sultan
E-mail: Randa.Abdullah.S@gmail.com

Areej Osama Mahjoub
E-mail: aomahjoub@gmail.com

Raghda Abdullah Sultan
E-mail: raghdasultan@hotmail.com

Abstract:
Vitamin D deficiency is one of the major public health problems for all age groups worldwide. It has many major roles in human body including normal growth. Vitamin D deficiency is significantly more prevalent in obese children, and in recent years, the prevalence of obesity has increased globally, and it is now one of the major universal health problems. Vitamin D deficiency can also compromise growth and lead to short stature. The aim of this study was to evaluate the impact of vitamin D deficiency on growth of children in Saudi Arabia. We conducted a cross-sectional study including 273 participants in which 193 were girls and 144 were boys aged 4 to 13 years. They were evaluated in an ambulatory pediatric clinic at King Abdul-Aziz university hospital in Jeddah, Saudi Arabia, between August 2016 and April 2017. Serum levels of vitamin D were evaluated in relation to body weight and height. The mean age among children in our study group was 9.9 ± 3.8 years. A prevalence rate of vitamin D deficiency of 96.7% was identified with 263 participants. Normal serum levels of vitamin D identified in only 3.3% of participants. Vitamin D levels were inversely related to body weight. For height no relation to vitamin D level was found. This study showed a significant effect of vitamin D deficiency on the incidence of obesity. As both vitamin D deficiency and obesity remain risk factors for developing diseases at later age. Increasing awareness, early prevention, and vitamin D supplementation should become a public health priority.
Key words: *Vitamin D, Obesity, Body-Weight, Height, Children*

1. INTRODUCTION

Vitamin D is also known as Calcitriol or 1, 25-Dihydroxycholecalciferol. Vitamin D has significant role in different physiological systems of human body. It has many major roles in human body including normal growth. Vitamin D is mainly considered for its role associated with the health of bones, teeth, and cartilages as well as calcium absorption, but Vitamin D is also essential for other mental and developmental functions. Vitamin D deficiency is one of the major public health problem for all age groups worldwide [1]. Vitamin D deficiency is significantly more prevalent in obese children. In recent years, the prevalence of obesity has increased, and now it is significantly one of the major global public health problem [2]. Vitamin D is one of the essential components which needs to be included in the daily diet. It is essential for activity and proper development of physiological systems of the human body. Vitamin D causes many health issues and diseases associated with the physical development, brain, thyroid glands, bones, teeth, and heart.

Vitamin is one of the vital components to be included in the diet on daily basis. It strengthens the bones and help in growth and developing by maintaining many physiological and biochemical processes. Vitamin D is also important for the absorption of calcium. It has been observed that calcium absorption is also compromised in case of vitamin D deficiency. There are multiple health related issues, which are associated with vitamin D deficiency. Vitamin D deficiency can also compromise growth and development and may lead to short stature. The term "short stature" is referred to two or more standard deviations of human body below the average height for the appropriate age, sex, and race [3]. Annweiler et al. (2010) stated that there is functional association of vitamin D with brain and many neurological activities [4]. Vitamin D is one of the fat-soluble vitamins and can be synthesized and bioactivated in the human body with sun exposure. The rich sources of vitamin D are fish, eggs, fortified milk, and cod liver oil [5]. Obesity is defined as a body mass index (BMI) greater than the 95th percentile for age and sex [6]. Although, deficiency of vitamin D has remained as a major public health issue, but there are not enough studies conducted on vitamin D deficiency among Saudian children.

Aim & Objectives of Research

The aim of this study is to investigate the impact of Vitamin D deficiency on children growth in Jeddah, Saudi Arabia.
The main objectives of this research are,

- To assess the association between vitamin D deficiency and obesity.
- To evaluate the link of deficiency of vitamin D with weight and height.

- To figure out the risk of obesity related to vitamin D deficiency.

Research Questions

This research seeks the answers of the below mentioned questions;

- What is the relationship between vitamin D deficiency and obesity?
- How does vitamin D deficiency relate to the weight and height?
- How can the obesity be developed due to deficiency of vitamin D?

Significance of the Study

This study has made a valuable contribution to the previous work done on the evaluation of the relationship between vitamin D deficiency and obesity. This study could help healthcare professionals while diagnosing causes of obesity in children. The relation of weight and height with vitamin D deficiency are also highlighted in the study supporting previous studies conducted in this context. This study may add a piece of informative work regarding the vitamin D deficiency in relation with the obesity in children in Saudi Arabia.

Limitations of the Study

This study cannot be generalized to all the population of the world. The reason is that this study has taken only children of Saudi Arabia. There are multiple factors such as environmental and genetic factors that can affect the association of the vitamin D with the obesity. That is why this study is limited to the population of Saudi Arabia.

2. METHODOLOGY

This study is based on the cross-sectional study design. Cross-sectional study design is widely used in the medical researches and studies related to social sciences. This study design is a type of observational study which involves the data collection from a population or a group of population and then data analysis is performed [7]. This type of study design may also include a characteristic subsection to estimated results at a specific point in time. The main purpose of selecting this study design is to evaluate descriptive issues. This method is mostly used to investigate and figure out the association between outcomes and experiences.

Participants

In this cross-sectional study, data was collected from 273 randomly selected healthy children. There were 193 girls and 144 boys aged in between 4 to 13 years. These participants were evaluated in an ambulatory pediatric clinic in King Abdul-Aziz University Hospital in Jeddah, Saudi Arabia, between August 2016 and April 2017. A questionnaire was designed to collect information on self-reported and direct measures of health and wellness. An interview was held with children and their family, followed by height and weight measurements. Phlebotomy team took blood samples for measurement of vitamin D, thyroid and parathyroid hormones, and calcium. Any child with organic disease (i.e. liver or kidney disease or diabetes mellitus), endocraniopathies, secondary obesity or secondary short stature, short stature (familial, genetic, malabsorption), supplementation with vitamin D or calcium, serious intercurrent illness and data insufficiency were excluded from the study.

Ethical Considerations

There are multiple ethical concerns that are significantly required to be considered while undertaking a study or research. Informed consent is one of the major ethical considerations while conducting research. It is regarding the permission, willingness, and understanding of the participants to take part in the study. It is quite essential that participants taking part in the research must have information about the purpose, process, potential benefits and risk related to study, as well as their alternative in participation in the study. Written and verbal consent were obtained prior to asking parents to fill in the questionnaire. Ethical approval for this study was obtained from the Research Ethics Committee at King Abdul-Aziz University Hospital (KAUH).

Weight and Height Variables

SDS was calculated for weight and height. Obesity was defined as weight SDS > 1.6, and short stature was defined as height SDS < 2. Log transformation was on weight which was measured in kilograms (kg) to transform positive skewed data of weight and to conform the normality at approximately level.

3. LABORATORY TESTS

Vitamin D Measurements

A fasting blood sample was drawn from participants. Vitamin D deficiency is the state of having a 25(OH)D concentration < 50 nmol/L (Lavie et al., 2014). For calcium level, a concentration of 2.2-2.62 mmol/L was considered normal. For evaluation of thyroid function, FT4 was assessed and a concentration of 12-22 pmol/L was taken as normal level. For parathyroid hormone, a concentration of 1.6-6.2 pmol/L was considered normal.

4. STATISTICAL ANALYSIS

Data analysis was performed using SPSS Statistics version 16.0 software (IBM Corp., Armonk, NY, USA). SPSS is widely used for analyzing the data collected from a research to interpret the results. Standard descriptive statistics were presented as percentages or mean ± SD. Paired t-test was performed to compare group variables. The Levene test for equality of variances was used to test the normal distribution of variables in the groups. ANOVA was used to analyze the differences among group means and their associated procedures. A value of $P < 0.05$ was considered statistically significant.

5. RESULTS

Relevant characteristics of study group and measured serum levels are reported in table 1. This study group consisted of 193 girls (57.3%) and 144 boys (42.7%). The mean age of the participants was 9.9 ± 3.8 years (95%) with confidence interval

(CI), (9.4 to 10.6). The average weight of the participants was 34.6 kg for boys and 33.1 for girls. Mean values for log 10 of weight was same i.e. 1.5 for boys and girls. The average height in 132.3 cm in boys and 132.6 cm in girls.

Serum level of 25(OH)D concentration < 50 nmol/L is indicative of vitamin D deficiency, the results are shown in Figure 1. Deficiency of vitamin D was identified in 96.7 % of participants, while there were only 3.3% of participants with a normal serum level of 25(OH)D. Mean level of Vitamin D was 27.04 ± 11.3 nmol/L which was about 95% (Confidence Interval = 25.7, 28.4). With respect to calcium, thyroid and parathyroid levels, levels of calcium were normal in 91.2% of participants. Levels of FT4 were normal in 84.1% of participants. Levels of parathyroid hormone were normal in 86.1% of participants.

The relationship between level of vitamin D and weight/ height is shown in Figure 2. The results reported that Log10 weight increases as vitamin D levels decreases. On the other hand, as vitamin D level decreases, no change in height was found. Vitamin D showed significant relation with weight. Low vitamin D levels showed increase in the weight with the correlation value of -0.231 for both genders which means that Vitamin D has weak and negative relationship with the body weight for both gender.

On the other hand, the P-value is estimates as 0.004, which is less than significance value of 0.05. It means that there is a significant relation of body weight and Vitamin D for both gender and decrease in Vitamin D level will affect the body weight of both male and female. For height, there was no significant relation with vitamin D with the correlation value of 0.01. The P-value was 0.913 for the relation of vitamin D and height of the children showing that there is no significant relation between the height and vitamin D. This data is presented in Table 1.

Table 1: *Baseline characteristics of study population.*

Age, Body Measurement and Vitamin	**Males Mean ± SD**	**Females Mean ± SD**
Age (year)	9.5 ± 3.4	10.3 ± 4.2
Weight (Kg)	34.7 ± 15.5	33.2 ± 14.2
Weight (sds)	1.4 ± 2.3	0.8 ± 1.8
Log10 Weight	1.5 ± 0.2	1.4 ± 0.1
Height (cm)	132.3 ± 17.8	132.6 ± 17.3
Height (sds)	-0.01±1.3	-0.1±1.1
BMI (kg/m2)	18.2 ± 3.7	17.7 ± 3.2
BMI (sds)	0.9 ± 1.2	0.6 ± 1.2
Vitamin D	28.5 ± 11.5	25.9 ± 11.01

Table 2: *Relation of Vitamin D with other factors.*

	Items	**P-value**	**Mean ± SD or (r)**
Body Measurements	Log10 Weight	0.004	(r= - 0.23)
	Height (cm)	0.91	(r= 0.01)
Gender	Male	0.06	28.5 ± 11.5
	Female	0.06	25.9 ± 11.02

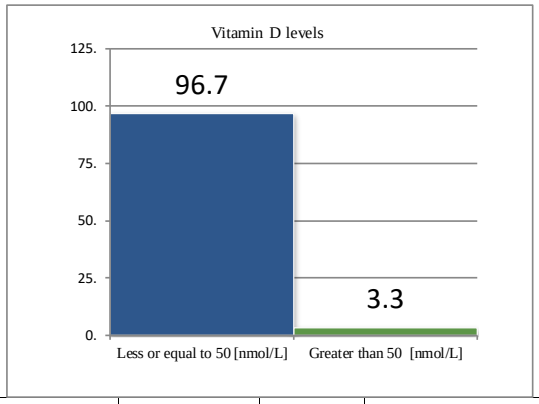
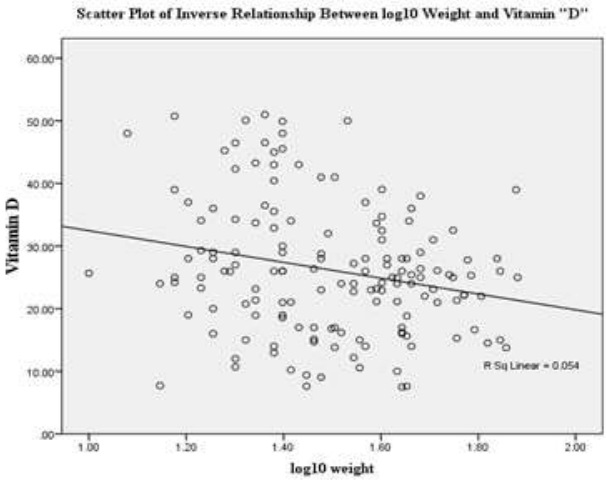


Figure 1: Vitamin D among population of the study



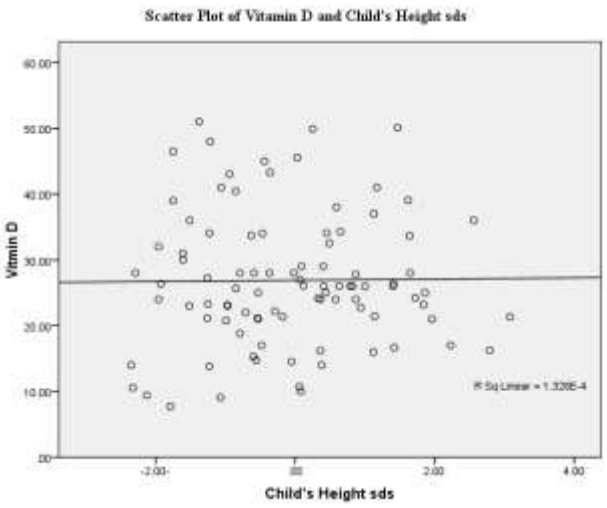


Figure 2 Vitamin D relation with height SDS

6. DISCUSSION

In this study, it has been investigated that there is a strong impact of vitamin D deficiency on children growth. A significant relation was found between vitamin D and weight, which directed toward the fact that low vitamin D levels increase weight and ultimately leads to obesity. There are multiple studies conducted worldwide on this issue to evaluate the relation between vitamin D deficiency and obesity. A study conducted in turkey showed that the prevalence of 25(OH)D deficiency was higher in the overweight and obese groups than in the normal weight groups and demonstrated link between decreased 25(OH)D levels and a high BMI [8].

Obesity is also observed in people suffering from vitamin D deficiency. It is suggested by some researches that low level of vitamin D is associated with the development of obesity, in addition to environmental and genetic factors and eating behaviors [9, 10, 11, 12]. Obesity has become a major health problem and its association with multiple serious complications including cardiovascular diseases, hypertension, diabetes mellitus which leads to high morbidity and mortality rates, affect the quality of life and cause social discrimination [11, 13, 14]. The impact of vitamin D deficiency on developing obesity is still under debate and researches are being conducted to evaluate the critical situation to overcome it [15].

The findings of this research revealed the importance of vitamin D and its association with obesity. For explanation of possible causes for the relation of vitamin D and obesity, several theories have been developed. One of them suggested that certain vitamin D receptor (VDR) polymorphisms are associated with obesity [16]. Another theory suggested that vitamin D is an essential factor for generation of leptin. Accordingly, depletion of vitamin D can take part in increasing the level of appetite resulting as obesity [17]. One of another experiment data has revealed that deficiency of vitamin D has role in increasing the process of lipogenesis by exaggerating the levels of parathyroid hormone facilitating calcium influx in adipocytes [18]. These theories and processes are also indicative of the relation of vitamin D and obesity.

An inverse association between vitamin D status and obesity was also reported in a study conducted in Kuala Lumpur [19]. The results of this research revealed that sub-optimal status of vitamin D are observed in the primary school children with obesity. Additionally, various epidemiological studies have demonstrated that vitamin D deficiency is closely related to obesity and increased risk of type 2 diabetes mellitus [20]. The results of an invitro study revealed that vitamin D plays a beneficial role in obesity progression, and that vitamin D deficient diet exacerbates weight gain. Similar results was reported in a preclinical research that high doses of vitamin D provided metabolic benefits such as increased insulin sensitivity and decreased body mass [21]. Another randomized clinical trial speculate that vitamin D supplementation may enhance weight reduction [22].

A study conducted by Kaseb, Haghighyfard, Salami, and Ghadiri-Anari (2017) revealed different results and reported no significant relationship between vitamin D deficiency and metabolic syndrome [23]. Frequency of vitamin D deficiency was 93.2% and the frequency of metabolic syndrome was 36 percent [23]. On the other hand, the relationship between vitamin D and height was not significant; low vitamin D level does not lead to short stature. Short stature can be attributed to several factors. One explanation of this can be need of a very low level of vitamin D < 10 ng/ml or 25 nmol/L to develop short stature. In accordance with the study population included in this study, only 107 (42%) had vitamin D levels below 25 nmol/L. Another important factor is calcium, which plays a major role in bone mineral density, and was found to be normal in most of the study subject. In contrast to results of this study, the relation between Vitamin D deficiency and short stature has been observed in a study conducted by Bueno, Czepielewski, and Raimundo (2010) in Brazil [24]. This study explored that low vitamin D intake was observed in short-stature children.

7. CONCLUSION

Vitamin D has significant impact on the physical and mental development of the human body. Deficiency of Vitamin D can raise different physiological and neurological issues. Vitamin D deficiency is among the most common public health issues at the global level. This study has shown a significant effect of low levels of vitamin D (Vitamin D deficiency) on the development of obesity. It is certain that deficiency of vitamin D in childhood may lead to different negative outcomes related to health in later stages of life. In accordance with the results of the study, the link of obesity and vitamin D has been evaluated. It can be stated that obesity and associated vitamin D deficiency are among the risk factors for developing different diseases and disorders in later age so it is required to spread awareness regarding this issue.

To prevent the society from this public health issue, it is essential to take care of the health patterns of the children and include vitamin D rich sources in their food. Early prevention and vitamin D supplementation can be helpful in this regards. Exposure to sunlight also impact significantly on the bioactivation and synthesis of vitamin D in human body. It is also essential to conduct more researches by defining more factors such as genetics, ethnicities, and races that can help in determining more accurate results. Many researches are conducted and being conducted but still there is need of more researches to be executed. These health issues must be taken into consideration and all the states and countries around the world should conduct the study to prevent the children and adults form vitamin D deficiency and its associated risks and complications.

8. REFERENCES

[1] Palacios, C. & Gonzalez, L. (2014). Is vitamin D deficiency a major global public health problem?. *The Journal of steroid biochemistry and molecular biology*, *144*, pp.138-145.

[2] Vanlint, S., 2013. Vitamin D and obesity. *Nutrients*, *5*(3), pp.949-956.

[3] Pandya, A., Aldouri, A., Pandya, N. & Bhaduri, B. (2010). A case series of vitamin D deficiency in mothers affecting their infants. *Infant*, *6*(6), 196.

[4] Annweiler, C., Schott, A.M., Allali, G., Bridenbaugh, S.A., Kressig, R.W., Allain, P., Herrmann, F.R. & Beauchet, O. (2010). Association of vitamin D deficiency with cognitive impairment in older women Cross-sectional study. *Neurology*, *74*(1), pp.27-32.

[5] Del Valle, H.B., Yaktine, A.L., Taylor, C.L. and Ross, A.C. eds. (2011). *Dietary reference intakes for calcium and vitamin D*. National Academies Press.

[6] Olson, M.L., Maalouf, N.M., Oden, J.D., White, P.C. & Hutchison, M.R. (2011). Vitamin D deficiency in obese children and its relationship to glucose homeostasis. *The Journal of Clinical Endocrinology & Metabolism*, *97*(1), 279-285.

[7] Setia, M.S. (2016). Methodology series module 3: Cross-sectional studies. *Indian journal of dermatology*, *61*(3), 261.

[8] Tosunbayraktar, G., Bas, M., Kut, A. & Buyukkaragoz, A.H. (2015). Low serum 25 (OH) D levels are associated to higher BMI and metabolic syndrome parameters in adult subjects in Turkey. *African health sciences*, *15*(4), 1161-1169.

[9] Mitchell, N., Catenacci, V., Wyatt, H.R. & Hill, J.O. (2011). Obesity: overview of an epidemic. *The Psychiatric clinics of North America*, *34*(4), 717.

[10] Nan, C., Guo, B., Warner, C., Fowler, T., Barrett, T., Boomsma, D., Nelson, T., Whitfield, K., Beunen, G., Thomis, M. & Maes, H.H. (2012). Heritability of body mass index in pre-adolescence, young adulthood and late adulthood. *European journal of epidemiology*, *27*(4), 247-253.

[11] Velásquez-Meléndez, G., Mendes, L.L. & Padez, C.M.P. (2013). Built environment and social environment: associations with overweight and obesity in a sample of Brazilian adults. *Cadernos de saude publica*, *29*(10), 1988-1996.

[12] Lavie, C. J., McAuley, P. A., Church, T. S., Milani, R. V., & Blair, S. N. (2014). Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. *Journal of the American College of Cardiology*, *63*(14), 1345-1354.

[13] Yao, Y., Zhu, L., He, L., Duan, Y., Liang, W., Nie, Z., Jin, Y., Wu, X. & Fang, Y. (2015). A meta-analysis of the relationship between vitamin D deficiency and obesity. *International journal of clinical and experimental medicine*, *8*(9), 14977

[14] Lazarevich, I., Irigoyen-Camacho, M.E. & Velázquez-Alva, M.D.C. (2013). Obesity, eating behaviour and mental health among university students in Mexico City. *Nutricion hospitalaria*, *28*(6).

[15] Creo, A.L., Rosen, J.S., Ariza, A.J., Hidaka, K.M. & Binns, H.J. (2013). Vitamin D levels, insulin resistance, and cardiovascular risks in very young obese children. *Journal of Pediatric Endocrinology and Metabolism*, *26*(1-2), 97-104.

[16] Wong, K.E., Kong, J., Zhang, W., Szeto, F.L., Ye, H., Deb, D.K., Brady, M.J. & Li, Y.C. (2011). Targeted expression of human vitamin D receptor in adipocytes decreases energy expenditure and induces obesity in mice. *Journal of Biological Chemistry*, *286*(39), 33804-33810.

[17] Kremer, R., Campbell, P.P., Reinhardt, T. & Gilsanz, V. (2009). Vitamin D status and its relationship to body fat, final height, and peak bone mass in young women. *The Journal of Clinical Endocrinology & Metabolism*, *94*(1), 67-73.

[18] Hjelmesæth, J., Hofsø, D., Aasheim, E.T., Jenssen, T., Moan, J., Hager, H., Røislien, J. & Bollerslev, J. (2009). Parathyroid hormone, but not vitamin D, is associated with the metabolic syndrome in morbidly obese women and men: a cross-sectional study. *Cardiovascular diabetology*, *8*(1), 7.

[19] Khor, G.L., Chee, W.S., Shariff, Z.M., Poh, B.K., Arumugam, M., Rahman, J.A. & Theobald, H.E. (2011). High prevalence of vitamin D insufficiency and its association with BMI-for-age among primary school children in Kuala Lumpur, Malaysia. *BMC public health*, *11*(1), 95.

[20] Li, Y.X. & Zhou, L. (2015). Vitamin D Deficiency, Obesity and Diabetes. *Cellular and molecular biology (Noisy-le-Grand, France)*, *61*(3), 35-38.

[21] Chang, E., & Kim, Y. (2017). Vitamin D insufficiency exacerbates adipose tissue macrophage infiltration and decreases AMPK/SIRT1 activity in obese rats. *Nutrients*, *9*(4), 338.

[22] Szlagatys-Sidorkiewicz, A., Brzeziński, M., Jankowska, A., Metelska, P., Słomińska-Frączek, M. & Socha, P. (2017). Long-term effects of vitamin D supplementation in vitamin D deficient obese children participating in an integrated weight-loss programme (a double-blind placebo-controlled study)–rationale for the study design. *BMC pediatrics*, *17*(1), 97.

[23] Kaseb, F., Haghighyfard, K., Salami, M. S., & Ghadiri-Anari, A. (2017). Relationship Between Vitamin D Deficiency and Markers of Metabolic Syndrome Among Overweight and Obese Adults. *Acta Medica Iranica*, *55*(6), 399-403.

[24] Bueno, A.L., Czepielewski, M.A. & Raimundo, F.V. (2010). Calcium and vitamin D intake and biochemical tests in short-stature children and adolescents. *European journal of clinical nutrition*, *64*(11), 1296.