

The Association between Overweight and Some Biological Markers among Fewer than 6 Years Aged Children

Hiba Muwafaq Saleem^{1*}, Thikra Majid Muhammed², Saleem Obaid Gatia Almawla³

^{1,2}Medical Laboratory Techniques Department, Al Maarif University College ,
Al-Anbar, Iraq

³Senior microbiologist in Maternity and Child Teaching hospital in Ramadi Iraq

Email ^{1*}: h.m.saleem@uoa.edu.iq , Email ²: th.m.mohammed@uoa.edu.iq,

Email ³: Almawla@gmail.com

ABSTRACT

Body mass index (BMI) is an important indicator of overweight and obesity in childhood and adolescence. When measurements are taken carefully and compared with appropriate growth charts and recommended cutoffs, BMI provides an excellent indicator of overweight and obesity that is sufficient for most clinical, screening, and surveillance purposes. Accurate measurements of height and weight require that adequate attention be given to data collection and management. Recent years have seen a rapid increase in the incidence of obesity in children and adolescents, leading to widespread concern. Obesity is a significant health problem world-wide, particularly in developed nations it is often associated with vitamin D deficiency and secondary hyperparathyroidism. The roles of vitamin D , and parathyroid hormone (PTH) are discussed controversially in obesity, and studies of these hormones in obese children are limited. Therefore, we studied the relationships between PTH, vitamin D (25-OH) , weight status, and calcium before and after level in Iraqi patients. Patients and Methods: This study assessed 45 overweight/obese children and 30 healthy (control) children. The distributions of Age , gender , serum 25-hydroxyvitamin D (25(OH)D) concentration PTH and calcium level were compared among different groups. Results: The serum 25-hydroxyvitamin D (25(OH)D) concentration , calcium level was significantly lower ($p < 0.05$) in overweight/obese children as compared with control group while the parathyroid hormone and body mass index was showed significantly higher ($p < 0.05$) in overweight/obese children as compared with control group. Conclusions: This studies was showed an association between calcium , parathyroid hormone and vitamin D with childhood obesity. So the Children with obesity have higher risk of vitamin D deficiency.

Keywords

parathyroid hormone; vitamin D; obesity; overweight

Introduction

Childhood obesity is top of mind for health professionals and the public because of heightened media attention about this issue. Obesity is now undoubtedly a growing worldwide health problem. Lifestyle behaviors and diet play an important role in developing childhood obesity (1)

Vitamin D is considered a prohormone, and must be metabolized to its hormonal form in order to function and it is an essential nutrient, is primarily involved in calcium homeostasis and bone mineralization. After entering systemic circulation via the skin or the lymph, vitamin D is cleared within hours via uptake by the liver or peripheral tissues, particularly adipose and skeletal muscle. The primary

role of vitamin D is in the development and maintenance of good bone health, through regulation of calcium and phosphorus homeostasis (2) In the absence of sufficient vitamin D, production of parathyroid hormone (PTH) is upregulated as a compensatory measure, resulting in secondary hyperparathyroidism.(3) Hypovitaminosis D and hyperparathyroidism are risk factors for bone loss(4)

Vitamin D deficiency and childhood obesity have been classified as epidemics throughout the world, and both share some common risk factors including poor diet and inactivity. Observational and clinical studies show that vitamin D status and fat mass are inversely correlated. It is not clear whether vitamin D deficiency contributes to, or is a consequence of obesity, or whether there are regulatory interactions between excess adiposity and vitamin D activity. The effects of this deficiency in childhood obesity appear to have negative influences on overall health, including insulin resistance, inflammation, and impeded bone mineralization, as well as increased future risk of type 2 diabetes, cardiovascular disease, and osteoporosis. The rather ubiquitous distribution of the vitamin D receptor and the 25-hydroxyvitamin D 1 α -hydroxylase throughout the body, including evidence for a role of vitamin D in adipogenesis and adipocyte metabolism, may in part explain these widespread effects. Most of the findings to date suggest that the vitamin D needs of obese children are greater than the non-obese. Although ultraviolet B-induced skin synthesis is a main source of vitamin D, its use is neither feasible nor prudent due to limited sun availability for many and concerns for skin cancer. Likewise, obtaining adequate vitamin D from natural food sources alone is generally not achievable, and even in countries that allow fortification, vitamin D intakes are low. Therefore, in obese children, vitamin D supplementation is warranted. Weight loss interventions using energy restriction and physical activity may also improve the poor vitamin D status associated with obesity. More research is needed to define optimal vitamin D status in this vulnerable population, including investigations to determine the efficacy of vitamin D supplementation in attenuating the conditions associated with childhood obesity, and to further elucidate the mechanisms by which vitamin D exerts its effects on health (4)

The synthesis and secretion of parathyroid hormone (PTH) is higher in those with vitamin D deficiency (5,6). Both PTH and 25OHD play important roles in calcium homeostasis (5).

Beside the parathyroid hormone and vitamin D, Calcium plays a role in many biological functions, especially in skeletal mineralization, as well as in muscle contraction and cell division in glycogen metabolism.(7) Calcium metabolism in the human body can be controlled by negative feedback mechanisms such as intestinal absorption, renal reabsorption, and bone storage.(8) Various hypotheses have been proposed regarding the metabolic effect of calcium on adipose tissue in the treatment of obesity.(9)

Patients and Methods

This study enrolled children(49 boys and 26 girls) from the general pediatric population who were under 6 years old. All patients included in the study were Iraqi children in Al-Ramadi Hospital in the period January 2021 to May 2021.

Blood testing

Fasting calcium serum levels were measured by colorimetric methods using a COBAS E411 analyzer (Roche Diagnostic, Mannheim, Germany). 25(OH)D levels were calculated by a high-specific chemiluminiscence-immunassay (LIAISON Assay, Diasorin, Dietzenbach, Germany), and PTH levels were determined by a highly specific solid-phase, two-site chemiluminescent enzyme-labeled immunometric assay using an Immulite analyzer (DPC Biermann, Bad Nauheim, Germany). In addition, we assessed the dynamics of annual BMI increments, defined as the change in BMI standard-deviation score per year, during childhood in 75 children.

Result and Discussion

Childhood obesity has both immediate and long-term effects on health. According to age and gender, this study was showed no significantly difference ($p < 0.05$) between overweight/obese children and control group.

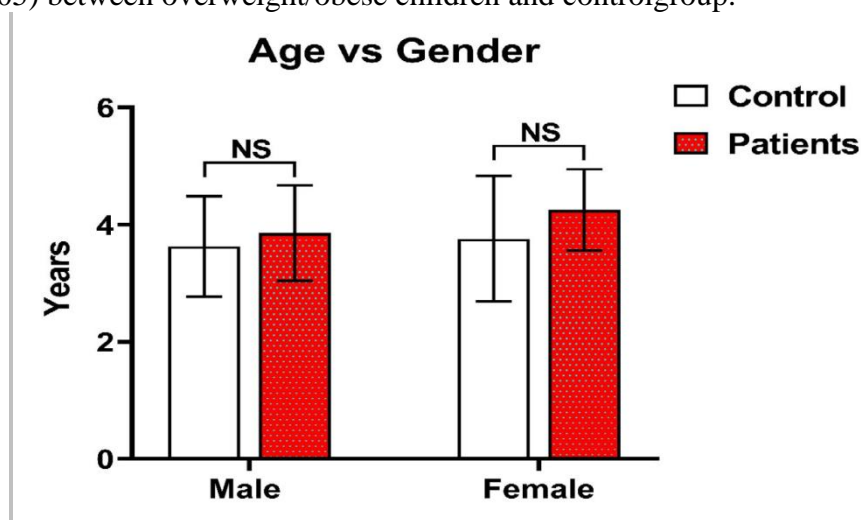


Figure (1) The comparison between the patients and control according to Age and Gender

While when we analyzing the result of samples according to BMI we observed there are a higher significantly differences ($p < 0.05$) in overweight/obese children as compared with control group

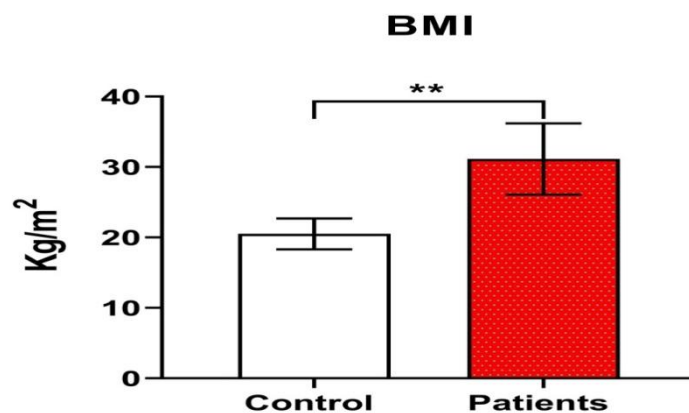


Figure (2) The comparison between the patients and control according to Body mass index

Previous studies found the temporal changes in BMI from age 3 years to 6 years are significantly associated with both environmental and behavioral factors at age 6 years. The results of this study may be useful for health promotion programs designed to prevent obesity during the early stages of childhood. (10) Increases in prevalence of overweight and obesity among both adults and children have been observed in many countries throughout the world (11, 12) Many obese children already manifest some metabolic complications, and these children are at high risk for the development of early morbidity. Understanding the underlying pathogenesis of this peculiar phenotype is of critical importance (13)

Vitamin D and parathyroid hormone (PTH) are well known for their essential role in bone metabolism and calcium homeostasis.

In this study the Obesity has been found to be associated with lower levels of serum 25-OH Vit D, Calcium and higher levels of serum PTH

when we analyzing the result of samples according to Vitamin D we observed there are a lower significantly differences ($p < 0.05$) in overweight/obese children as compared with control group

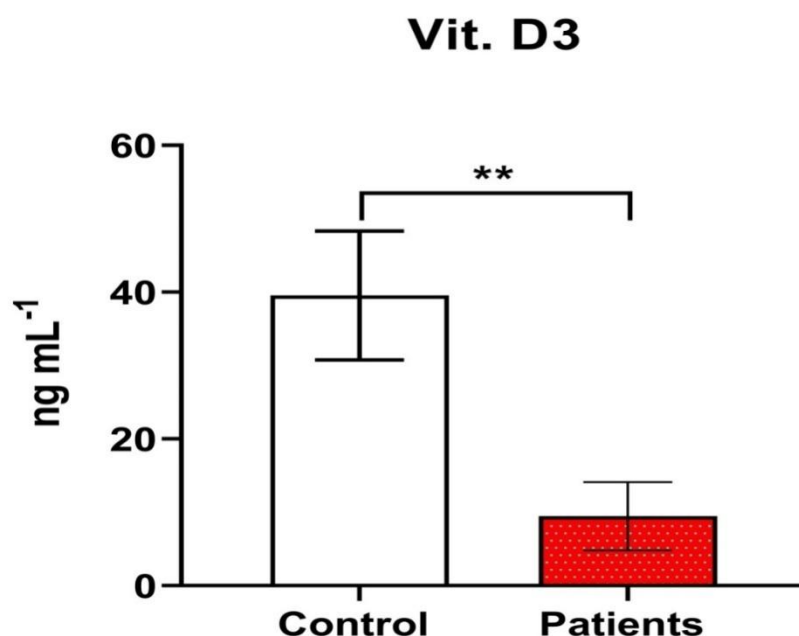


Figure (3) The level of 25-hydroxy-vitamin D in obese and normal weight children

A low vitamin D intake was associated with increased body mass index (BMI) (14)

The low levels of 25-OH Vit D in obese children in our study are in concordance with most studies in adults (15,16,17)

The higher vitamin D levels in normal weight subjects seem to be more a surrogate parameter for healthy nutrition than a real causal factor in the prevention of obesity. Intervention studies in obese children with vitamin D supplementation are necessary to prove this hypothesis. Furthermore, the low levels of 25-OH Vit D may be attributed to several other factors such as decreased exposure to sunlight in obese subjects due to limited mobility, clothing habits, or the excessive deposition of vitamin D in adipose tissue (18,19)

Some studies reported other factors associated with vit D deficiency. Khor *et al.* demonstrated higher prevalence of vit D deficiency in girls (77.5%) than boys (66.1%), with statistical significance ($p < 0.01$). Rajakumaret *al.* show there was evidenced lower prevalence of hypovitaminosis D in individuals with white skin color, and in the summer and autumn seasons.

While in figure (4) when we analyzing the result of samples according to Parathyroid hormone we observed there are a higher significantly differences ($p < 0.05$) in overweight/obese children as compared with control group

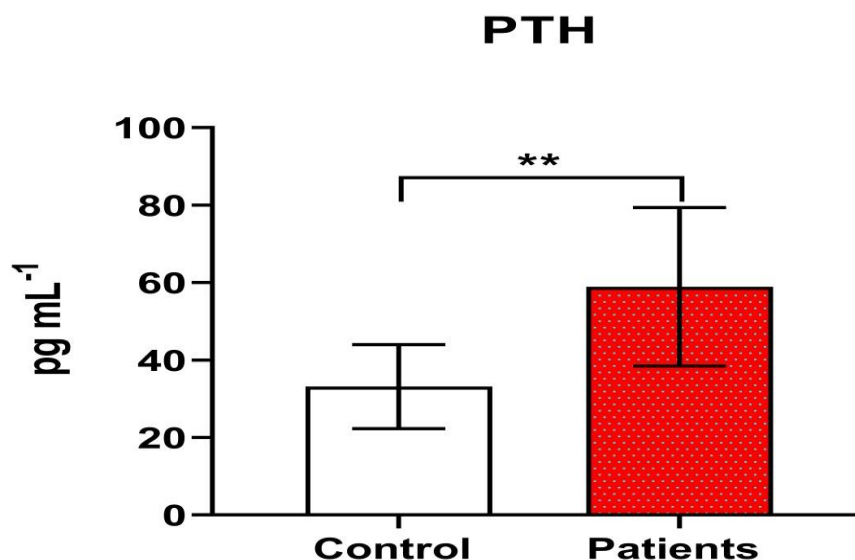


Figure (4) The level of Parathyroid hormone in obese and normal weight children

Parathyroid hormone has been postulated as an independent predictor of obesity. Since patients with primary or secondary hyperparathyroidism were heavier than those in the control group, it has been postulated that increased PTH levels contribute towards obesity (22, 23, 24).

PTH stimulates the renal hydroxylation of 25-OH Vit D to its active form, 1,25-OH Vit D, which in turn elevates the calcium influx into adipocytes. In these cells, intracellular calcium enhances lipogenesis through the activation of fatty acid synthase and inhibits lipolysis via activation of phosphodiesterase 3B, which subsequently reduces catecholamine-induced lipolysis (25, 26, 27)

Both these effects would promote lipid storage in fat tissue. Additionally, studies support a direct role for PTH in suppressing lipid oxidation in the muscle (28)

However, these hypotheses are discussed controversially since in obese adults with weight loss, increasing and decreasing 25-OH Vit D as well as decreasing and increasing PTH concentrations have been reported (29, 30) so that the question whether the alterations of these hormones are a consequence or cause of overweight remains open.

And when we analyzing the result of samples according to Calcium level we observed there are a lower significantly differences ($p < 0.05$) in overweight/obese children as compared with control group

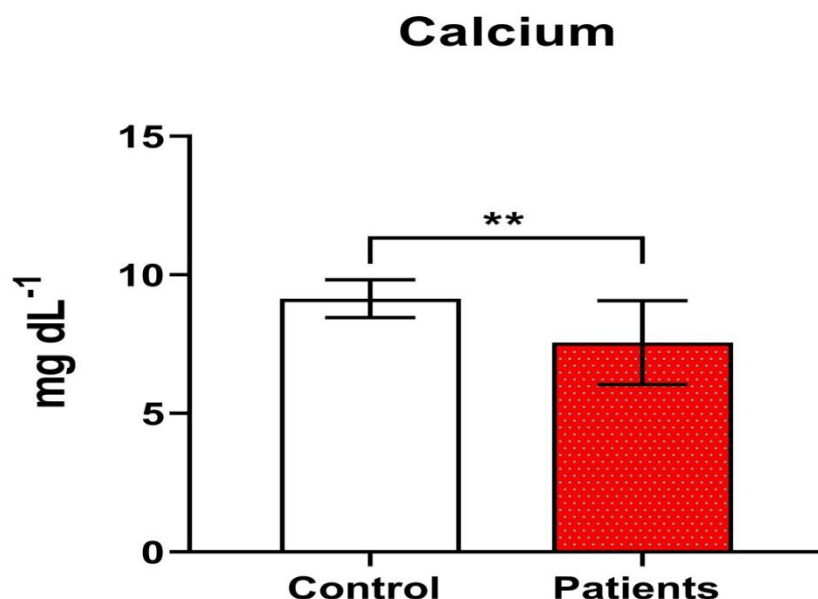


Figure (5) The level of Calcium in obese and normal weight children

This can be explained by the role of calcitriol in calcium absorption. Calcitriol influences active transport by increasing membrane permeability, regulating calcium migration through the intestinal cells and increasing the levels of calbindin. The fraction of absorbed calcium increases as its intake decreases, due to a partial adaptation to this micronutrient restriction, resulting in increased active transport mediated by calcitriol. Thus, the active transport becomes the main mechanism of calcium absorption when its ingestion is low. (31)

Other studies have associated the role of calcium in obesity to the effect of this micronutrient on fecal excretion of fat and appetite regulation. Dietary calcium and calcium supplements may increase the fecal excretion of fat by forming insoluble complexes in the intestine (32)

However, studies have shown that this effect is relatively small (especially with calcium supplements).(33 , 34)

Du, *Xet al* . suggested that a low supply of both vitamin D and calcium contribute to the etiology of vitamin D deficiency and both deficiencies should be corrected .Thus, this mechanism contributes to the antiobesity effect of calcium, but cannot explain it fully (32,33 ,36)It is suggested that calcium intake may interfere with appetite regulation; however, this effect was assessed in only a few studies and the hypothesis has not been confirmed. So It can be observed that many of the mechanisms that explain adiposity and its association with the assessed micronutrients demonstrate the close association between calcium and the vitamin D present in the metabolic eventsof adipogenesis, and the fact that the presence or absence of one of them can bring damage not only to bone, but health as a whole. The mechanisms involved in the association between obesity and serum levels of vitamin D have not been described specifically for children. (37) Figure 6 shows the possible mechanisms involved in the association between vitamin D and obesity

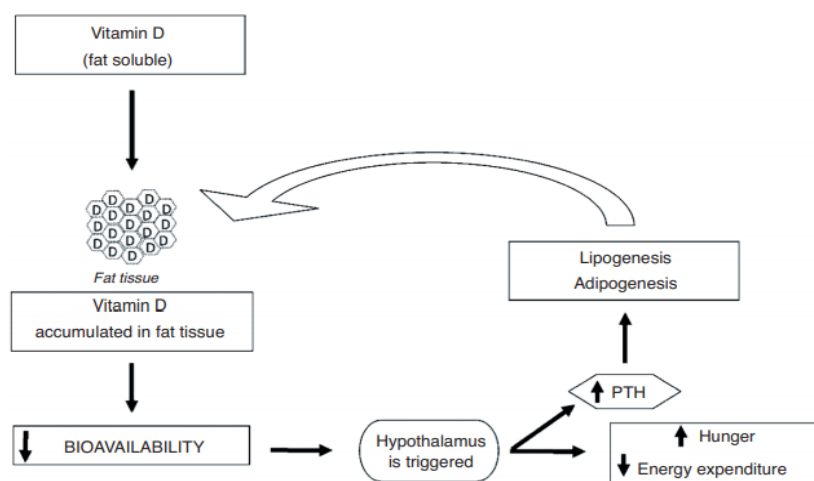


Figure (6) The cyclical association between vitamin D deficiency and increased body fat deposition.

Conclusions

This study showed there are an association between calcium and vitamin D with childhood obesity. Considering the possible protective effect of these micronutrients in relation to childhood obesity, preventive public health actions should be designed, with emphasis on nutritional education

References

1. ABD-Elrahman, N. A., El Marasy, S. S., Tawfik, A. A. E. F., Elsayd, H. H., & Aboraya, A. O. (2021). THE RELATION BETWEEN OBESITY AMONG PRESCHOOL CHILDREN AND QUALITY OF THEIR DIETARY INTAKE. *Plant Archives*, 21(1), 666-671.
2. Institute of Medicine. Food and Nutrition Board. Dietary reference intakes for calcium and vitamin D. Washington, D.C.: National Academies Press; 2011.
3. Muscogiuri G, Sorice G, Giaccari A, et al. 25-Hydroxyvitamin D concentration correlates with insulin-sensitivity and BMI in obesity. *Obesity*. 2010;18(10):1906-1910.
4. Peterson, C. A. (2015). Vitamin D deficiency and childhood obesity: interactions, implications, and recommendations. *Nutrition and Dietary Supplements*, 7, 29-39.
5. Holick, M. The Vitamin D Epidemic and its Health Consequences. *J. Nutr.* 2005, 135, 27395–27485.
6. Bilezikian, J.P.; Marcus, R.; Levine, M.A.; Marcocci, C.; Silverberg, S.J.; Potts, J.T. *The Parathyroids: Basic and Clinical Concepts*; Academic Press: London, UK, 2014.
7. Pravina, P., Sayaji, D., & Avinash, M. (2013). Calcium and its role in human body. *International Journal of Research in Pharmaceutical and Biomedical Sciences*, 4(2), 659-668.
8. Peacock, M. (2010). Calcium metabolism in health and disease. *Clinical Journal of the American Society of Nephrology*, 5(Supplement 1), S23-S30.
9. Yıldız, N. (2015). Kadınlar da diyetle farklı miktarlardaki kalsiyum tüketiminin ağırlık kaybı ve bazı antropometrik ölçümler üzerine etkisi (Master's thesis, Başkent Üniversitesi Sağlık Bilimleri Enstitüsü).

10. Sugimori, H., Yoshida, K., Izuno, T., Miyakawa, M., Suka, M., Sekine, M., ... & Kagamimori, S. (2004). Analysis of factors that influence body mass index from ages 3 to 6 years: a study based on the Toyama cohort study. *Pediatrics International*, 46(3), 302-310.
11. Silventoinen, K., Sans, S., Tolonen, H., Monterde, D., Kuulasmaa, K., Kesteloot, H., & Tuomilehto, J. (2004). Trends in obesity and energy supply in the WHO MONICA Project. *International journal of obesity*, 28(5), 710-718.
12. Wang, Y., Ge, K., & Popkin, B. M. (2000). Tracking of body mass index from childhood to adolescence: a 6-y follow-up study in China. *The American journal of clinical nutrition*, 72(4), 1018-1024.
13. Cali, A. M., & Caprio, S. (2008). Obesity in children and adolescents. *The Journal of Clinical Endocrinology & Metabolism*, 93(11_supplement_1), s31-s36.
14. Kamycheva, E., Joakimsen, R. M., & Jorde, R. (2003). Intakes of calcium and vitamin D predict body mass index in the population of Northern Norway. *The Journal of nutrition*, 133(1), 102-106.
15. Parikh, S. J., Edelman, M., Uwaifo, G. I., Freedman, R. J., Semega-Janneh, M., Reynolds, J., & Yanovski, J. A. (2004). The relationship between obesity and serum 1, 25-dihydroxy vitamin D concentrations in healthy adults. *The Journal of Clinical Endocrinology & Metabolism*, 89(3), 1196-1199.
16. D'Auria, E., Barberi, S., Cerri, A., Boccardi, D., Turati, F., Sortino, S., ... & Ciprandi, G. (2017). Vitamin D status and body mass index in children with atopic dermatitis: A pilot study in Italian children. *Immunology letters*, 181, 31-35.
17. Fiamenghi, V. I., & de Mello, E. D. (2020). Vitamin D deficiency in children and adolescents with obesity: a meta-analysis. *Jornal de Pediatria. overweight and obese US children. Pediatrics*, 131(1), e152-e161.
18. Arunabh, S., Pollack, S., Yeh, J., & Aloia, J. F. (2003). Body fat content and 25-hydroxyvitamin D levels in healthy women. *The Journal of Clinical Endocrinology & Metabolism*, 88(1), 157-161.
19. Wortsman, J., Matsuoka, L. Y., Chen, T. C., Lu, Z., & Holick, M. F. (2000). Decreased bioavailability of vitamin D in obesity. *The American journal of clinical nutrition*, 72(3), 690-693.
20. 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), 1-8.
21. Rajakumar, K., de Las Heras, J., Chen, T. C., Lee, S., Holick, M. F., & Arslanian, S. A. (2011). Vitamin D status, adiposity, and lipids in black American and Caucasian children. *The Journal of Clinical Endocrinology & Metabolism*, 96(5), 1560-1567.
22. Stein, M. S., Flicker, L., Scherer, S. C., Paton, L. M., O'Brien, M. L., Walton, S. C., ... & Wark, J. D. (2001). Relationships with serum parathyroid hormone in old institutionalized subjects. *Clinical endocrinology*, 54(5), 583-592.
23. Bolland, M. J., Grey, A. B., Gamble, G. D., & Reid, I. R. (2005). Association between primary hyperparathyroidism and increased body weight: a meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*, 90(3), 1525-1530.
24. Grey, A. B., Evans, M. C., Stapleton, J. P., & Reid, I. R. (1994). Body weight and bone mineral density in postmenopausal women with primary hyperparathyroidism. *Annals of internal medicine*, 121(10), 745-749.

25. Zemel, M. B., Shi, H., Greer, B., Dirienzo, D., & Zemel, P. C. (2000). Regulation of adiposity by dietary calcium. *The FASEB Journal*, 14(9), 1132-1138.
26. McCarty, M. F., & Thomas, C. A. (2003). PTH excess may promote weight gain by impeding catecholamine-induced lipolysis-implications for the impact of calcium, vitamin D, and alcohol on body weight. *Medical hypotheses*, 61(5-6), 535-542.
27. Shi, H., DiRienzo, D., & Zemel, M. B. (2001). Effects of dietary calcium on adipocyte lipid metabolism and body weight regulation in energy- restricted aP2- agouti transgenic mice. *The FASEB journal*, 15(2), 291-293.
28. Smogorzewski, M., Perna, A. F., Borum, P. R., & Massry, S. G. (1988). Fatty acid oxidation in the myocardium: effects of parathyroid hormone and CRF. *Kidney international*, 34(6), 797-803.
29. TEITELBAUM, S. L., HALVERSON, J. D., BATES, M., WISE, L., & HADDAD, J. G. (1977). Abnormalities of circulating 25-OH vitamin D after jejunal-ileal bypass for obesity: evidence of an adaptive response. *Annals of internal medicine*, 86(3), 289-293.
30. Slater, G. H., Ren, C. J., Siegel, N., Williams, T., Barr, D., Wolfe, B., ... & Fielding, G. A. (2004). Serum fat-soluble vitamin deficiency and abnormal calcium metabolism after malabsorptive bariatric surgery. *Journal of Gastrointestinal Surgery*, 8(1), 48-55.
31. Dawson-Hughes, B. E. S. S., Harris, S. S., & Finneran, S. U. S. A. N. (1995). Calcium absorption on high and low calcium intakes in relation to vitamin D receptor genotype. *The Journal of Clinical Endocrinology & Metabolism*, 80(12), 3657-3661.
32. Zemel, M. B. (2005). The role of dairy foods in weight management. *Journal of the American College of Nutrition*, 24(sup6), 537S-546S.
33. Jacobsen, R., Lorenzen, J. K., Toubro, S., Krog-Mikkelsen, I., & Astrup, A. (2005). Effect of short-term high dietary calcium intake on 24-h energy expenditure, fat oxidation, and fecal fat excretion. *International journal of obesity*, 29(3), 292-301.
34. Christensen, R., Lorenzen, J. K., Svith, C. R., Bartels, E. M., Melanson, E. L., Saris, W. H., ... & Astrup, A. (2009). Effect of calcium from dairy and dietary supplements on faecal fat excretion: a meta- analysis of randomized controlled trials. *Obesity reviews*, 10(4), 475-486.
35. Du, X., Greenfield, H., Fraser, D. R., Ge, K., Trube, A., & Wang, Y. (2001). Vitamin D deficiency and associated factors in adolescent girls in Beijing. *The American journal of clinical nutrition*, 74(4), 494-500.
36. Major, G. C., Chaput, J. P., Ledoux, M., St- Pierre, S., Anderson, G. H., Zemel, M. B., & Tremblay, A. (2008). Recent developments in calcium- related obesity research. *Obesity reviews*, 9(5), 428-445.
37. Cunha, K. A. D., Magalhães, E. I. D. S., Loureiro, L. M. R., Sant'Ana, L. F. D. R., Ribeiro, A. Q., & Novaes, J. F. D. (2015). Calcium intake, serum vitamin D and obesity in children: is there an association?. *Revista Paulista de Pediatria*, 33(2), 222-229.