Meta-analysis of Vitamin D Supplementation trials in Deficient Children Suffering from Obesity

Thesis

Systematic Review / Meta-Analysis for Partial Fulfilment of Master Degree in Clinical Nutrition

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا

إلا ما علمتنا إنك أنت

العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Dedication

الحمد لله رب العالمين حمدا كثيرا الحمد لله على نعمه التي لا تحصى ولا تعد

الحمد لله حتى يبلغ الحمد منتهاه

I dedicate this work to my late mother **Dr Alia El-Bestar** and my late father **Professor Fouad Nassar.** Although long gone they are still the inspiration and the driving force to every successful event in my life.

My next dedication goes to my beloved family. The actual support that I received from my **husband Judge Ahmed Rageh** and **daughter Aya** is beyond words. They were there for me throughout all the steps and shared my burden in a memorable way that would always keep me indebted to them.

Acknowledgment

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Last but not least I would like to thank all the young boys and girls trying to control their weight in the Clinical Nutrition Clinic, Paediatric Department, Ain Shams University and wish them all the best of health. It was their struggle that inspired me to do this meta-analysis. I just hope that the conclusion and recommendations of this study can help them reach their goals easier.

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List of Abbreviations

Abb.	Full term
25 (OH) D	25 hydroxy vitamin D
ADHD	Attention deficit hyperactivity disorder
BAI	Body adiposity index
BMI	Body mass index
Ca	Calcium
CCT	Controlled clinical trial
CDC	Centres for Disease Control and Prevention
CRP	C-reactive protein
CVD	Cardiovascular disease
FBT	Family-based multicomponent behavioural weight loss treatment
FNB	Food and Nutrition Board
IBD	Inflammatory bowel disease
IOM	Institute of Medicine's
IOTF	International Obesity Task Force
NAFLD	Non-alcoholic fatty liver disease
OSAS	Obstructive sleep apnea syndrome
PTH	Parathyroid hormone
RCT	Randomized controlled clinical trial
RDA	Recommended dietary allowance
UL	Tolerable upper intake level
UVB	Ultra violet B rays
VD	Vitamin D
VDR	Vitamin D receptor
WHO	World Health Organization

INTRODUCTION

Both childhood obesity and vitamin D deficiency are common in the Middle East. Additionally, the body adiposity index (BAI) is significantly associated with 25-hydroxyvitamin D [25(OH)D] levels in Arab children ***(Al-Daghri et al., 2016)***. Among the possible determinants of low vitamin D status in preschool children in the Makkah region were high body mass index (BMI), inadequate vitamin D intake, and low levels of outdoor physical activity ***(Kensarah et al., 2015)***.

As early as intrauterine life this problem may show. Vitamin D deficiency in pregnancy may increase the risk of prenatal and early postnatal overweight offspring ***(Morales et al., 2015)***. There is increasing evidence of an association between low vitamin D and a range of non-bone health outcomes, however there is a lack of data from robust randomised controlled trials on vitamin D supplementation ***(Paxton et al., 2013)***. ***Williams et al. (2014)*** suggested that obese children should be considered for routine vitamin D screening.

Szlagatys-Sidorkiewicz et al. (2017) stated that vitamin D supplementation may enhance weight reduction and prevent bone loss in obese children with this deficiency. ***Brinkmann et al. (2015)*** warned against weight excess which interferes with the response to vitamin D supplementation, leading to attenuated increase in 25(OH)D even with supplementation.

On the basis of a bi-directional genetic approach that limits confounds, ***Vimaleswaran et al. (2013)*** concluded that a high BMI leads to low 25(OH)D, while any effects of low 25(OH)D increasing BMI are likely to be small. The latter authors further added that population-level interventions to reduce BMI are expected to decrease the prevalence of vitamin D deficiency.

AIM OF THE WORK

The main objective of the current systematic review/meta-analysis was to compare the effect of vitamin D supplementation in deficient children and adolescents suffering from obesity.

The secondary objective was to compare the effectiveness of supplementary doses of vitamin D in obese children compared to adolescents and in obesity versus overweight.

Chapter 1
PAEDIATRIC OBESITY

Definitions

Obesity is a condition of excess adiposity and the most common measurement used in its diagnosis is body mass index (BMI; weight in kilograms divided by the square of height in meters). The World Health Organization (WHO) ***(de Onis et al., 2007)***, US Centers for Disease Control and Prevention (CDC) ***(Ogden et al., 2012)*** and the International Obesity Task Force (IOTF) ***(Cole et al., 2000)*** each have different cut-offs in defining paediatric obesity. For instance, CDC considers a BMI greater than or equal to the 95th percentile on the BMI-for-age growth charts to be indicative of obesity ***(Ogden et al., 2012)***, while WHO defines paediatric obesity as a BMI greater than two standard deviations above the WHO growth standard median ***(de Onis et al., 2007)***.

Damanhoury et al. (2018) provided a consensus-based definition of the metabolically healthy obesity needed for clinical decision-making for children with obesity and it included: high density lipoprotein-cholesterol > 40 mg/dl (or > 1.03 mmol/l), triglycerides ≤ 150 mg/dl (or ≤ 1.7 mmol/l), systolic and diastolic blood pressure ≤ 90th percentile, and a measure of glycaemia.

Epidemiology of childhood and adolescent obesity

Obesity has reached global dimensions, and prevalence of childhood obesity has increased eightfold since 1975 ***(Weihrauch-Blüher and Wiegand, 2018)***. Obesity, in addition to the alarming problem of stunting, has become a trend and measures to prevent both challenges have been highlighted by ***Nassar (2017)*** under the slogan "Defying secular trend". ***Al-Refaee et al. (2012)*** reported that childhood overweight was high in Kuwait and increased with age. Overweight and obesity affected 19% to 21% of school-aged children from Lebanon and KSA as reported by ***Nasreddine et al. (2018)***.

Causes and risk factors of obesity in paediatric age group

A recent systematic review by ***Albataineh et al. (2018)*** concluded that several dietary behaviours such as missing breakfast, excessive fat and refined carbohydrate intake with low micronutrient intake due to low consumption of fruits, vegetables and milk/diary, are associated with obesity in children in the Middle East. Additionally, high consumption of soft drinks has been associated with lower intakes of milk and calcium-rich foods and higher body mass index among Kuwaiti children in a study done by ***Nassar et al. (2104)***.

Recently, evidence-based studies have shown that the duration of exclusive breastfeeding and the type of complementary feeds during the weaning period of an infant may have an effect on over-nutrition later on in life. Thus, stemming the tide of obesity early on in life would potentially decrease the prevalence and complications of adult obesity, which could have significant implications for health care and the economy at large ***(Laving et al., 2018)***. The latter authors added that although the relationship between complementary feeding and childhood obesity has been suspected for a long time, specific risk parameters are not as firmly established. Early introduction of complementary feeds (before the 4th month of life), high protein and energy content of feeds, and nonadherence to feeding guidelines may be associated with overweight and obesity later in life.

Porter et al. (2018) identified modifiable risk factors associated with severe obesity in children ages 5 and younger and these are:

- Nutrition (consuming sugar sweetened beverages and fast food),
- Activity (low frequency of outdoor play and excessive screen time),
- Behaviours (lower satiety responsiveness, sleeping with a bottle, lack of bedtime rules, and short sleep duration),
- Socio-environmental risk factors (informal child care setting, history of obesity in the mother, and gestational diabetes).