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Vitamin D Deficiency and Metabolic Sindroms: Literature Review

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ABSTRACT
Based on current research, lack of micronutrients, especially Vitamin D, is thought to be associated with metabolic disorders. A good understanding of vitamin D deficiency as a risk factor for metabolic disorders is the basis for establishing policies and programs
Search for articles in literature review through Scientdirect, PubMed, Medline, and Google Scholar were publication periods between 2010-2019.
Vitamin D/serum 25 (OH) D levels is associated with obesity, hypertention, glycemia index but studies relating vitamin D deficiency and lipid profiles have not shown consistent results. Most of research found association of Vitamin D and Metabolic Syndrome (MetS)
Based on the review, most of the study results indicate that Vitamin D is associated with parameters in the metabolic syndrome, so that Vitamin D could be a new risk factor for MetS.

Keywords: Vitamin D, Metabolic Syndrome, Profil lipid, Glicemic Index, Hypertension

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BACKGROUND

The success of Indonesia's national development cannot be separated from the quality of human resources, so that improving the quality of human resources is part of the development goals. However, the impact of Non-Communicable Diseases (PTM) on the resilience of human resources is very large because in addition to being a cause of death and illness it also reduces productivity.

Based on the results of Riskesdas, the death rate due to NCD (Non Comunicable Disease) increased from 41.7% in 1995 to 49.9% in 2001 and 59.5% in 2007. The highest cause of death from all causes of death was stroke (15.4%), followed by hypertension, diabetes, cancer, and chronic obstructive pulmonary disease (Riskesdas, 2010). Based on the results of Riskesdas, there was an increase in the prevalence of these diseases in people aged> 15 years, where the prevalence of diabetes mellitus increased from 6.9% to 8.5% and hypertension in people aged ≥ 18 years increased from 25.8% to 34 , 1% (Balitbangkes, 2019).

This metabolic disease, associated with obesity, is where obesity is increasing rapidly worldwide. In Indonesia, the prevalence of obesity continues to increase from 10.7% (2010), 14.8% (2013) to 21.8% (2018). Currently, metabolic disease is associated with excessive body weight and an inactive lifestyle.

However, research is currently developing that lack of micronutrients, especially Vitamin D, is also allegedly related to these metabolic disorders. In fact, various studies abroad, both in sub-tropical and tropical countries, show that the prevalence of vitamin D deficiency is quite high. A survey by SEANUTS (South East Asian Nutrition Surveys) in 48 districts in Indonesia shows that vitamin D intake at the age of 9-12 years is 50.6% insufficient, 46.8% inadequate and only 2.5% is desirable (Seanuts Indonesia, 2011).
The purpose of this paper is to determine the relationship between vitamin D and metabolic syndrome (MetS) and its parameters (central adiposity, triglycerides, HDL cholesterol, blood pressure, plasma glucose concentration). A good understanding of vitamin D deficiency as a risk factor for metabolic disorders is the basis for establishing policies and programs

METHODS

Search for articles in this literature review through Scientdirect, PubMed, Medline, and Google Scholar by using the keywords "Vit D, metabolic syndroms, obesity, profil lipid, glicemic index and or hypertension" The inclusion criteria used in this study were Indonesian or English with publication periods between 2010-2019. Appropriate articles will be noted in the table.

RESULTS

Definition of Metabolic Syndrome (MetS) and Vitamin D Deficiency

Metabolic syndrome (MetS) is a multiplex risk factor arising from insulin resistance that accompanies abnormal adipose deposition and function. It consists of a combination of risk factors for coronary heart disease, as well as diabetes, fatty liver, and some types of cancer. Clinical manifestations of metabolic syndrome include hypertension, hyperglycemia, hypertriglyceridemia, decreased HDL-C, abdominal obesity, chest pain or shortness of breath cardiovascular complications, acanthosis nigricans, hirsutism, peripheral neuropathy, and retinopathy in patients with insulin resistance and hyperglycemia or with diabetes mellitus, xanthomas. or xanthelasmas in patients with severe dyslipidemia (Eckel, 2011).

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The diagnostic criteria for Metabolic Syndrome (MetS) were established by the International Diabetes Federation (IDF) organization. Someone categorized has the metabolic syndrome if he or she has central adiposity plus two or more of the following factors (6): 1) Concentration of triglycerides: ≥150 mg / dl or specific treatment for this lipid abnormality 2) Concentration of HDL cholesterol: <40 mg / dl in men and <50 mg/dl in women or specific treatment for this lipid abnormality; 3) Blood pressure: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or treatment of previously diagnosed hypertension; and 4) Fasting plasma glucose concentration ≥100 mg/dl or previously diagnosed type 2 diabetes (IDF, 2006).

While the definition of Vitamin D Deficiency (VDD), The Society for Adolescent Health and Medicine (SAHM) considers a serum 25 (OH) D concentration> 30 ng / mL (75 nmol /L) to be sufficient and is an indication of normal vitamin D status.The SAHM considers a serum 25 (OH) D concentration of 30 to 30.50 ng/mL (75 125 nmol /L) is optimal for adolescents (more concentrations pose a health risk) (Harel *et al.*, 2013).

This review is based on the results of research studies, meta analyzes, review articles assessing the relationship between Vitamin D / 25 (OH) D and the components of the metabolic syndrome namely obesity, lipid profile (TG, TC, LDL-C, HDL-C) in adolescents, children as well as adults. The results of reviews summarized in the following table:

Research Summary, Journal Reviews, Articles on the Relationship of Vitamin D Vitamin D Supplementation and Metabolic Syndrome

NO	SOURCES	JOURNAL	SAMPLE	DESIGN	MEASUREMENT	RESULTS
1.	(Muscogiuri *et al.*, 2010)	Obesity (2010) 18, 1906–1910	n= 39 (18 male and 21females)	Experiment	Insulin, PTH concentration, 25(OH)D), electrolytes and total cholesterol,HDL and LDL cholesterol	BMI was predictor of insulin-sensitivity. There is no cause–effect relationship between vitamin D and insulin-sensitivity.
2	(Belenchia *et al.*, 2013)	American Journal Clinical Nutrition (Am J Clin Nutr 2013;97:774–81)	n=35 (obese adolescent patients	Randomized controlled trial	Vit D3 concentration, inflammatory markers (IL-6, TNF-α, C-reactive protein), leptin, adiponectin, fasting glucose, fasting insulin, & HOMA-IR	Participants supplemented with Vit D3 had increases in serum 25(OH)D concentrations, fasting insulin, HOMA-IR and leptin-to-adiponectin ratio
3.	(Liu *et al.*, 2016)	Clinica Chimica Acta (2016)	n=443 (children and adolescents)	Cross Sectional	Serum 25 (OH)D], lipid and glucose and obesity	Obese children and adolescents are more likely to have lower

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						concentrations of serum 25(OH)D
4.	(Cheng, 2018)	Journal of Pediatric Nursing 38 (2017) 20–26	Children (6–12 years) with obesity vit D & insufficiency	Meta-analysis	Obesity, Vit D Deficiency (VDD), lifestyle	Obesity was risk factor for VDD.
5.	(Schmitt *et al.*, 2018)	Maturitas Volume 107, Januar y 2018, Pages 97-102	n = 463 women, (45–75 years)	Cohort study	TC, HDL, LDL, triglycerides, glucose, insulin and [25(OH)D]	Women with VDD had a higher risk of MetS, hyperTG and low HDL than those with adequate levels.
6.	(Al-Dabhani *et al.*, 2017)	Nutrition & Diabetes vol ume 7, page 263 (2017)	n = 1205 (702 women and 503 men 18 - 80 years old	Cross-sectional study	Vit D level, MetS	Metabolic syndrome was associated with presence of VDD
7.	(Kelishadi, Farajzadeg an and Bahreynia, 2014)	Int J Food Sci Nutr, 2014; 65(4): 404–410	n = 25.394 subjects of 17 cross-sectional studies	Systematic review and meta-analysis	Serum 25(OH)D, triglycerides, TC, HDL-C	There are significant association between 25(OH)D and triglycerides), total cholesterol and HDL-C
8.	(Erol *et al.*, 2017)	Arch Argent Pediatr 2017;115(2): 133-139	n = 108 (obese children)	Cross Sectional	Serum TG, TC, LDL-C, HDL-C, fasting glucose, insulin, alanine aminotransfera se, Vit D levels	The dyslipidemic obese children, 94.87% had insulin resistance; the vitamin D levels were <20 ng/ml in 69.3% of them
9.	(Cabral *et al.*, 2016)	Internationa l Journal of Cardiology 220 (2016) 501–507	n = 1033 adolescent	Cross-sectional	Serum 25(OH)D levels and metabolic syndrome (MetS) features	There is a significant increase in TC and LDL-C for lower 25(OH)D levels and an increased odds of high BMI for those with a lower Vit D intake, no association between Vit D levels and MetS

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10.	(Reis *et al.*, 2009)	Pediatrics 2009;124;e 371	n = 3577 (12-19 years)	Cross-sectional	25 (OH) D levels, MetS parameters	Low serum vitamin D is strongly associated with hypertension, hyperglycemia, and MetS
11.	(Challa, Makariou and Siomou, 2015)	Pediatr Endocr Met 2015	-	Review Article	Vit D status, MetS parameters	Insufficient vitamin D status is associated with increased prevalence of MetS and its components (blood pressure and IR)
12.	(Forouhi *et al.*, 2008)	The Medical Research Council (2008)	n=524 (man and woman aged 40-69 year)	Kohort Prospektif Study	Serum 25(OH)D, glycemic status, [ipids, insulin, anthropometry, and blood pressure measured and MetS risk (MetS z score)	Baseline 25(OH)D was associated risk of hyperglycemia , insulin resistance, HOMA-IR and metabolic syndrome z score

DISCUSSION

Vitamin D and Obesity

Based on the following table, it can be seen that vitamin D deficiency is associated with obesity ((Erol *et al.*, 2017), (Liu *et al.*, 2016), (Cheng, 2018), (Cabral *et al.*, 2016). Liu found that serum 25 (OH) D and insufficient vitamin D were higher in obese children than non-obese children. High BMI is more common in those with low vitamin D intakes (Cabral *et al.*, 2016).There is strong evidence that obesity is a risk factor for vitamin D deficiency (Muscogiuri *et al.*, 2010), (Cheng, 2018). (Muscogiuri *et al.*, 2010) also showed that BMI was the strongest predictor of low 25 (OH) D concentrations. According to (Belenchia *et al.*, 2013) vitamin D is associated with insulin resistance. It is estimated that vitamin D is also associated with metabolic syndrome (Makariou *et al.*, 2011).

Vitamin D and Lipid Profiles

Studies relating vitamin D deficiency and lipid profiles have not shown consistent results. A meta-analysis study by (Kelishadi, Farajzadegan and Bahreynian, 2014) found that high serum 25 (OH) D was associated with a better lipid profile in children, however the study of (Cabral *et al.*, 2016) who observed total cholesterol (TC) and LDL in reducing levels of 25 (OH)D, did not show a significant relationship. (Erol *et al.*, 2017) in his research on vitamin D deficiency and insulin resistance as risk factors for dyslipedemia in obese children found that vitamin D deficiency was a risk factor for dyslipidemia. (Liu *et al.*, 2016)(Schmitt *et al.*, 2018) suggest that those who are deficient in Vitamin D have higher levels of cholesterol and triglycerides than those who are sufficiently Vitamin D. (Schmitt *et al.*, 2018) also found women with VDD had a higher risk low HDL than those with adequate levels.

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Vitamin D and Hypertension

Research on vitamin D and cardiometabolic risk factors in adolescents shows that low serum vitamin D is strongly associated with hypertension (Reis *et al.*, 2009). Likewise, a review article by (Challa, Makariou and Siomou, 2015)suggests that vitamin D insufficiency is associated with the prevalence of blood pressure metabolic syndrome. and insulin resistance, often independent of obesity and abdominal adipocytes.Vitamin D is also significantly predicted as another risk factor for metabolic syndrome (Erol *et al.*, 2017) (Liu *et al.*, 2016),

Vitamin D and Glycemia Index

Meanwhile, the effect of vitamin D on the glycemic index is shown by (Reis *et al.*, 2009) and (Rashidi, Ghaderian and Moradi, 2018). (Reis *et al.*, 2009) stated that serum vitamin D in US adolescents is strongly associated with hyperglycemia and metabolic syndrome. Likewise research by Forouhi, et. al (2008) 14 in a 10-year cohort study showed that serum vitamin D levels were associated with glucose levels in the future.

Vitamin D and Metabolic Syndrome (MetS)

Challa et. al (2015), (Schmitt *et al.*, 2018), (Al-Dabhani *et al.*, 2017), (Reis *et al.*, 2009) showed that vitamin D insufficiency is associated with the prevalence of metabolic syndrome, but (Cabral *et al.*, 2016) found there was no no association between Vit D levels. (Forouhi *et al.*, 2008) said 25(OH)D was associated risk of metabolic syndrome z score.

CONCLUCION

Based on this review, most of the study results indicate that Vitamin D/serum 25 (OH) D is associated with parameters in the metabolic syndrome, so that Vitamin D could be a new risk factor for many chronic diseases, such as the MetS.

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