

Is Metabolic Syndrome a Long Term Effect of Stunting? : A Literature Review

Muhammad Harits^a, Nur Aisiyah Widjaja^b, Meity Ardiana^c

^a *Medicine Programme, Universitas Airlangga, Surabaya, Indonesia*

^b *Department of Pediatric, Universitas Airlangga, Surabaya, Indonesia*

^c *Department of Cardiovascular, Universitas Airlangga, Surabaya, Indonesia*

Abstract

Stunting is a condition resulted from inadequate nutritional intake for a long period. It is a sign of a persistent growth disease in which a child's health and nutritional issues prevent him from growing to his full height. Maternal nutritional status, breastfeeding habits, supplementary feeding routines, and virus exposure are factors that may have contributed to stunting. The presence of three of the five criteria for the metabolic syndrome—central obesity, hyperglycemia, hypertriglyceridemia, high density lipoprotein, and hypertension—is required. Stunting has short-term effects like increased morbidity and mortality, impaired cognitive and motor development, higher health care costs, and long-term effects like short stature, increased risk of obesity and other chronic diseases, risk of degenerative disease, and poorer reproductive health. Because there is a greater chance that a chronic condition may emerge, metabolic syndrome is thought to be one of the long-term effects of stunting (obesity, diabetes, heart and blood vessel disease, stroke, cancer and disability in old age). Obesity was caused by nutritional stunting, which impeded fat oxidation. The higher systolic blood pressure is also associated to hypertension. Children who are undernourished are more likely to develop central obesity due to low-grade inflammation brought on by extra visceral fat. Loss of lean mass and subcutaneous fat also contributes to metabolic dysregulation of insulin-stimulated glucose uptake and the development of metabolic syndrome.

Keywords : Stunting; Metabolic Syndrome

1. Introduction

1.1. Stunting

Stunting is a condition of chronic malnutrition caused by inadequate nutritional intake for a long time. This condition could be the result of feeding habits that do not adhere to the guidelines for proper nutrition in support of the child's growth and development according to age. [1] According to WHO anthropometric criteria, stunting is determined by dividing each child's Z-score by their age. By comparing a child's height or length to the average height of children their own age and sex in the general community, stunting conditions can be found. The term "stunting condition" refers to a chronic development disease in which a child's potential height is not reached because of dietary and medical issues. [2]

Malnutrition in childhood has been linked to a higher incidence of obesity in adulthood. [3] Malnutrition is linked to increased risk of metabolic disease in adults, impaired physical function, neurodevelopmental capacity, and morbidity and death. [4] Stunting has complicated effects that are influenced by a number of variables, including the local environment, food, and timing of developmental stages. [5] According to a study by Grillo et al. (2016), people with stunting have changed HDL cholesterol at much greater rates. [6] Numerous factors influence intrauterine development retardation, such as short mother stature, a low prenatal BMI, and a low pregnancy weight gain. [7] Nutritional deficits, high infection rates, and poor feeding techniques used by caregivers are the most prominent causes of postnatal growth retardation. Lack of one or

more nutrients, such as energy, protein, or micronutrients like iron, zinc, and vitamins D, A, or C, can lead to growth failure. Growth retardation is a symptom of phosphorus and zinc deficiency particularly. [8] By reducing food intake, reducing nutrient absorption, and increasing nutrient requirements, recurrent illness exacerbates pre-existing deficits. Growth retardation brought on by repeated infections and nutritional deficits is more likely to result in morbidity and mortality. The availability of sufficient care, time, attention, and support to address the physical, mental, and social needs of the developing kid has an impact on both nutrient intakes and health. The caregiver's training, beliefs, workload, time availability, health, and nutritional state are all crucial. [9]

1.2. Metabolic syndrome

The prevalence of metabolic syndrome is increasing in both children and adolescents. [10] The presence of three out of the five criteria for metabolic syndrome—central obesity, hyperglycemia, hypertriglyceridemia, high density lipoprotein, and hypertension—was established by the National Cholesterol Education Program (NCEP) in 2001. Type 2 diabetes mellitus, insulin resistance (on clamp), or impaired fasting glucose (110-125 mg/dL) plus two out of four criteria are the criteria used by WHO to define metabolic syndrome. WHR > 0.9 for men and > 0.85 for women, or BMI > 30 kg/m², were considered central obesity. Systolic blood pressure of more than 140 mmHg or diastolic blood pressure of less than 90 mmHg was considered hypertension. Urinary albumin excretion was defined as less than 20 mcg/min, while hypertriglyceridemia was classified as TG 150 mg/dL. Metabolic syndrome is a concept with several element, including physiological, biochemical, clinical and metabolic factors that directly increase the risk of atherosclerosis, type 2 DM, and all cause mortality. [11] The pathogenesis of metabolic syndrome suggested that interaction of obesity, insulin resistance and inflammation is significant to development. Accumulation of free fatty acids in the liver, adipocytes, skeletal muscles and the pancreas in the setting of obesity leads to impaired insulin signaling and subsequent insulin resistance. Clinical features in metabolic syndrome shows as symptoms of obesity, dyslipidemia, hypertension, glucose intolerance and T2DM, non alcoholic fatty liver disease, polycystic ovarian syndrome and increased production of inflammatory cytokines by the visceral adipocytes. [12]

1.3. Is Metabolic Syndrome a Long Term Effect of Stunting?

Children with stunts are shorter than their peers and look two to three years younger. It is also associated with developmental delay and delayed achievement of key developmental milestones in children, such walking. A developmental impairment that begins very early in life is present with stunting. Although the growth phase can be extended until ages 20 to 22, the developmental delay may not be enough to make up for the initial growth deficit. [13] Stunting's immediate effects could lead to an increase in morbidity and death, delayed cognitive and motor development, and higher health care costs. [14] Long term impact of stunting could cause inadequate body posture so that the children are shorter than normal children, and the risk of obesity and other diseases increases, reproductive health decreases, learning capacity and performance during school time become insufficient, leading to inadequate productivity and work. [15]

Children who are stunted are more likely to acquire chronic diseases, have impaired fat oxidation that results in obesity, and have decreased glucose tolerance. [16] A research by Hoffman et al. (2000) found that nutritional stunting is strongly associated with poor fat oxidation, which leads to more fat being retained in adipose tissue. The hormones and enzymes in charge of fat oxidation have been compromised by long-term undernutrition. [17] Stunting during the first two years of life was linked to higher systolic blood pressure at the age of 7-8 years, according to a study by Gaskin et al. [18] Indirectly, stunting raises the risk of

degenerative diseases. Stunting children are more likely to develop obesity, diabetes, heart and blood vessel disease, stroke, cancer, and long-term impairment. [19]

According to reports, central obesity is more common in undernourished, stunted adults. [20] However, rather than examining particular fat compartments, the majority of studies rely on anthropometric measures of body fat. Due to the increased secretion of multiple pro-inflammatory cytokines, which may play a significant role in many diseases by promoting angiogenesis, inflammation, cell proliferation, and insulin resistance, visceral fat is associated with low grade inflammation. [21-23] In some populations, subcutaneous fat may be a useful predictor of unfavorable metabolic effects. [24] After accounting for current BMI, DeLucia et al(2018) found a connection between early stunting and increased visceral fat deposition in adulthood. Additionally, it is linked to a loss of lean mass, the buildup of subcutaneous belly fat, and the bulk of total body fat. [25]. Subcutaneous fat loss is brought on by consuming insufficient amounts of food that is low in calories and protein. [26]. When it comes to metabolic syndrome, this body composition profile could be harmful.

The largest insulin-sensitive tissue in the body is lean mass, which is important for preserving glucose metabolism. [27-28] The development of the metabolic syndrome is facilitated by decreased lean mass, which altered glucose homeostasis, including metabolic dysregulation of insulin-stimulated glucose uptake. [29] Independent of abdominal fat, low lean mass has been demonstrated to be one of the most significant risk factors for metabolic syndrome in adults. [30] The development of insulin resistance in lean mass has been linked to increased accumulation of adipose tissue and intramuscular fat, dysregulated production of inflammatory adipokines, increased renin angiotensin aldosterone system activity, and decreased mitochondrial oxidative phosphorylation flux in the muscle. [29] Reduced subcutaneous fat may also cause fat to build up in other tissues and organs. Fat tissues such visceral adipose tissue, the pancreas, muscle, and liver may store fat if fat cell production in the subcutaneous fat compartment fails when body fat levels rise. [31] This excessive storage could be linked to insulin resistance, glucose intolerance, and diabetes as well as the poor distribution of belly fat and hepatic steatosis. [32]

1.4. Conclusion

Stunting caused by insufficient nutrition has a variety of long- and short-term effects, including an increase in morbidity and mortality, delays in cognitive and motor development, and higher medical expenses. Stunting has long-term effects such as short stature, increased risk of obesity and other chronic diseases, risk of degenerative diseases, and poor reproductive health. Because nutritional stunting decreased fat oxidation and led to obesity, metabolic syndrome is thought to be one of the long-term effects of stunting. The higher systolic blood pressure is also associated to hypertension. Children who are undernourished are more likely to develop central obesity due to low-grade inflammation brought on by extra visceral fat. Loss of subcutaneous fat and lean mass also plays role in metabolic dysregulation of insulin stimulated glucose uptake, hence causing metabolic syndrome.

References

- [1] Fatima S, Manzoor I, Joya AM, Arif S, Qayyum S. Stunting and associated factors in children of less than five years: A hospital-based study. *Pakistan journal of medical sciences*. 2020 Mar;36(3):581.
- [2] Wirth JP, Rohner F, Petry N, Onyango AW, Matji J, Bailes A, de Onis M, Woodruff BA. Assessment of the WHO Stunting Framework using Ethiopia as a case study. *Maternal & child nutrition*. 2017 Apr;13(2):e12310.

- [3] Sawaya AL, Martins P, Hoffman D, Roberts SB. The link between childhood undernutrition and risk of chronic diseases in adulthood: a case study of Brazil. *Nutrition reviews*. 2003 May 1;61(5):168-75.
- [4] Martins PA, Hoffman DJ, Fernandes MT, Nascimento CR, Roberts SB, Sesso R, Sawaya AL. Stunted children gain less lean body mass and more fat mass than their non-stunted counterparts: a prospective study. *British Journal of Nutrition*. 2004 Nov;92(5):819-25.
- [5] Tanner S, Leonard WR, Reyes-García V, TAPS Bolivia Study Team. The consequences of linear growth stunting: influence on body composition among youth in the Bolivian Amazon. *American journal of physical anthropology*. 2014 Jan;153(1):92-102.
- [6] Grillo LP, Gigante DP, Horta BL, De Barros FC. Childhood stunting and the metabolic syndrome components in young adults from a Brazilian birth cohort study. *European Journal of Clinical Nutrition*. 2016 May;70(5):548-53.
- [7] Ramakrishnan U, Manjrekar R, Rivera J, Gonzáles-Cossío T, Martorell R. Micronutrients and pregnancy outcome: a review of the literature. *Nutrition research*. 1999 Jan 1;19(1):103-59.
- [8] Golden MH. The role of individual nutrient deficiencies in growth retardation of children as exemplified by zinc and protein. In *Nestle nutrition workshop series (USA)* 1988.
- [9] Engle PL, Menon P, Haddad L. Care and nutrition: concepts and measurement. *World Development*. 1999 Aug 1;27(8):1309-37.
- [10] Ogden CL, Carroll MD, Lawman HG, Fryar CD, Kruszon-Moran D, Kit BK, Flegal KM. Trends in obesity prevalence among children and adolescents in the United States, 1988-1994 through 2013-2014. *Jama*. 2016 Jun 7;315(21):2292-9.
- [11] Al-Hamad D, Raman V. Metabolic syndrome in children and adolescents. *Translational pediatrics*. 2017 Oct;6(4):397.
- [12] Balkau B, Vernay M, Mhamdi L, Novak M, Arondel D, Tichet J, Eschwege E, DESIR Study Group. The incidence and persistence of the NCEP (National Cholesterol Education Program) metabolic syndrome. The French DESIR study. *Diabetes & metabolism*. 2003 Nov 1;29(5):526-32.
- [13] Branca F, Ferrari M. Impact of micronutrient deficiencies on growth: the stunting syndrome. *Annals of nutrition and metabolism*. 2002;46(Suppl. 1):8-17
- [14] Prendergast AJ, Humphrey JH. The stunting syndrome in developing countries. *Paediatrics and international child health*. 2014 Nov 1;34(4):250-65.
- [15] Martins VJ, Toledo Florêncio TM, Grillo LP, Franco MD, Martins PA, Clemente AP, Santos CD, Vieira MD, Sawaya AL. Long-lasting effects of undernutrition. *International journal of environmental research and public health*. 2011 Jun;8(6):1817-46.
- [16] Beal T, Tumilowicz A, Sutrisna A, Izwardy D, Neufeld LM. A review of child stunting determinants in Indonesia. *Maternal & child nutrition*. 2018 Oct;14(4):e12617.
- [17] Hoffman DJ, Sawaya AL, Verreschi I, Tucker KL, Roberts SB. Why are nutritionally stunted children at increased risk of obesity? Studies of metabolic rate and fat oxidation in shantytown children from Sao Paulo, Brazil. *The American journal of clinical nutrition*. 2000 Sep 1;72(3):702-7.
- [18] Gaskin PS, Walker SP, Forrester TE, Grantham-McGregor SM. Early linear growth retardation and later blood pressure. *European journal of clinical nutrition*. 2000 Jul;54(7):563-7.
- [19] Eckhardt CL. Micronutrient malnutrition, obesity, and chronic disease in countries undergoing the nutrition transition: potential links and program/policy implications. 2006.
- [20] Bennett F, Watson-Brown C, Thame M, Wilks R, Osmond C, Hales N, Barker D, Forrester T. Shortness at birth is associated with insulin resistance in pre-pubertal Jamaican children. *European journal of clinical nutrition*. 2002 Jun;56(6):506-11.
- [21] Finelli C, Sommella L, Gioia S, La Sala N, Tarantino G. Should visceral fat be reduced to increase longevity?. *Ageing research reviews*. 2013 Sep 1;12(4):996-1004.
- [22] Lebovitz HE, Banerji MA. Point: visceral adiposity is causally related to insulin resistance. *Diabetes care*. 2005 Sep 1;28(9):2322-5.

- [23] Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity?. Current opinion in endocrinology, diabetes, and obesity. 2012 Apr;19(2):81.
- [24] Lovejoy JC, Smith SR, Rood JC. Comparison of regional fat distribution and health risk factors in middle-aged white and African American women: the Healthy Transitions Study. Obesity research. 2001 Jan;9(1):10-6.
- [25] De Lucia Rolfe E, de França GV, Vianna CA, Gigante DP, Miranda JJ, Yudkin JS, Horta BL, Ong KK. Associations of stunting in early childhood with cardiometabolic risk factors in adulthood. PloS one. 2018 Apr 11;13(4):e0192196.
- [26] Kumari V, Abbas AK, Fusto N, Aster JC (2010) Environmental and Nutritional Diseases. Robbins and Robbins & Cotran Pathologic Basis of Disease. 8th ed. Philadelphia: Saunders Elsevier. pp. 438–443.
- [27] DeFronzo RA, Jacot E, Jequier E, Maeder E, Wahren J, Felber JP. The effect of insulin on the disposal of intravenous glucose: results from indirect calorimetry and hepatic and femoral venous catheterization. Diabetes. 1981 Dec 1;30(12):1000-7.
- [28] Baron AD, Brechtel G, Wallace P, Edelman SV. Rates and tissue sites of non-insulin-and insulin-mediated glucose uptake in humans. American Journal of Physiology-Endocrinology And Metabolism. 1988 Dec 1;255(6):E769-74.
- [29] Park BS, Yoon JS. Relative skeletal muscle mass is associated with development of metabolic syndrome. Diabetes & metabolism journal. 2013 Dec 12;37(6):458-64.
- [30] Atlantis E, Martin SA, Haren MT, Taylor AW, Wittert GA. Inverse associations between muscle mass, strength, and the metabolic syndrome. Metabolism. 2009 Jul 1;58(7):1013-22.
- [31] Pasarica M, Xie H, Hymel D, Bray G, Greenway F, Ravussin E, Smith SR. Lower total adipocyte number but no evidence for small adipocyte depletion in patients with type 2 diabetes. Diabetes care. 2009 May 1;32(5):900-2.
- [32] Kursawe R, Eszlinger M, Narayan D, Liu T, Bazuine M, Cali AM, D'Adamo E, Shaw M, Pierpont B, Shulman GI, Cushman SW. Cellularity and adipogenic profile of the abdominal subcutaneous adipose tissue from obese adolescents: association with insulin resistance and hepatic steatosis. Diabetes. 2010 Sep 1;59(9):2288-96.