Blood Vitamin D Levels in Hypercholesterolemic Patients

Dessy Hermawan[1*)]; Nova Muhani[2]; Syafiq Arisandi [3]

[1*)]PSIK Fakutas Kedokteran Universitas Malahayati Bandar Lampung
[2]Fakultas Kedokteran Universitas Malahayati Bandar Lampung
[3]Fakultas Kesehatan Masyarakat Universitas Malahayati Bandar Lampung

ARTICLE INFO

A B S T R A C T

The prevalence of hypercholesterolemia in Indonesia is currently still high, even though hypercholesterolemia is correlated with non-communicable diseases such as hypertension, heart disease, diabetes mellitus and so on. Recent studies have reported an association between low levels of vitamin D and increased cholesterol levels. This is interesting, if it is true that vitamin D is related to cholesterol levels, then people who live in tropical areas like Indonesia, should have low cholesterol levels. The purpose of this study was to analyze the relationship between vitamin D levels and total cholesterol levels in medical students of Malahayati University class of 2017. The design of this research is an analytical survey with a case control approach. The case sample was a total of medical students class 2017 who suffered from hypercholesterolemia as many as 26 people. The control sample was 26 students who had normal cholesterol levels, so the total sample was 52 students. The results showed that there was a significant relationship between cholesterol levels and blood vitamin D levels (0.005), Body Mass Index/BMI (0.001), waist circumference (0.005), exercise regularity (0.016) and outdoor activity habits (0.001). Suggestion: it is necessary to maintain vitamin D levels in the blood by consuming foods containing vitamin D and being active and exercising outdoors to be exposed to ultraviolet B rays from the sun.

A B S T R A K

Prevalensi hiperkolesterolemia di Indonesia, saat ini masih tinggi, padahal hiperkolesterolemia berkorelasi dengan penyakit tidak menular seperti hipertensi, penyakit jantung, diabetes mellitus dan sebagainya. Penelitian terbaru melaporkan adanya hubungan antara rendahnya kadar vitamin D dengan peningkatan kadar kolesterol. Hal ini menarik, jika benar vitamin D berhubungan dengan kadar kolesterol, maka seharusnya orang-orang yang tingggal di daerah tropis seperti Indonesia, akan memiliki kadar kolesterol yang rendah. Tujuan penelitian ini adalah untuk memperlajari hubungan antara kadar vitamin D dengan kadar kolesterol total pada mahasiswa kedokteran Universitas Malahayati angkatan 2017. Design penelitian ini adalah survey analitik dengan pendekatan case control. Adapun sampel kasus adalah total mahasiswa kedokteran angkatan 2017 yang mengalami hiperkolesterolemia sebanyak 26 orang dan yang menjadi sampel kontrol adalah 26 mahasiswa yang memiliki kadar kolesterol normal, sehingga total sampel sebanyak 52 orang. Hasil penelitian menunjukkan adanya hubungan yang bermakna antara kadar kolesterol dengan kadar vitamin D (0.005), Indeks Massa Tubuh/IMT (0.001), lingkar perut (0.005), keteraturan olah raga (0.016) dan kebiasaan beraktifitas di luar ruangan (0.001). Sedangkan jenis kelamin dan besaran uang jajan tidak berhubungan secara bermakna dengan kadar kolesterol. Saran: perlu menjaga kadar vitamin D dalam darah dengan mengkonsumsi makanan mengandung vitamin D dan berakatifitas serta berolah raga di luar ruangan agar terpapar sinar ultraviolet B dari sinar matahari.

INTRODUCTION

Hypercholesterolemia or high cholesterol levels in the blood is one of the triggering factors for non-communicable diseases (Sarkar & Roy, 2017), such as obesity, hypertension, diabetes mellitus, heart disease and others(Besseling, Kastelein, Defesche, Hutten, & Hovingh, 2015; Navar-Boggan et al., 2015). Currently, non-communicable diseases are a problem throughout the world, including in Indonesia.Based on a report from the Basic Health Research in 2018, the number of cases of hypercholesterolemia at the age of more than 15 years, is still relatively high, at 34.8%, slightly decreased when compared to the results of basic health research in 2013 which showed that 35.9% of the Indonesian population had cholesterol abnormalities. (Kementrian Kesehatan Republik Indonesia, 2018)

In theory, many factors can affect cholesterol levels in the human body, including age, physical activity(Heart Association, 2018), genetics, obesity, dietary fiber intake, the habit of eating fatty foods and other disease-related factors(Gibbs, 2018).The body mass index factor is also one of the factors that affect cholesterol levels in the body(Hubková et al., 2018). Cholesterol levels in men and women increase with an increase in body mass index/BMI. Research in China shows that the prevalence of hypercholesterolemia in both men and women is above 50% and the prevalence of being overweight is more than 30%(Rao et al., 2016).Research in Nigeria also reported an association between blood cholesterol levels and BMI even in the pediatric population (Nwaiwu & Ibe, 2015).

Recently, many studies have reported that hypercholesterolemia is also associated with a deficiency of vitamin D levels in the blood(Jiang, Peng, Chen, Wu, & Zhang, 2019; Mosca et al., 2019). The results of the study explain that vitamin D can reduce body fat by lowering parathyroid hormone and increasing blood calcium (Vanlint, 2013). Increased blood calcium will increase sympathetic nerve activity so that it will increase body heat production. This condition will cause an increase in the destruction of fat in the tissue.This mechanism is believed to be able to explain how vitamin D is able to lower cholesterol levels in the body.Although the actual mechanism is still much debated and still raises many questions.

This condition is interesting to be studied more deeply, is it true that low blood vitamin D levels are related to hypercholesterolemia?Vitamin D is a fat-soluble vitamin, vitamin D can be stored and taken back from the fat tissue of our body.Vitamin D plays an important role in maintaining serum calcium and phosphorus in normal conditions, also joint functions in the mineralization of bones and teeth and plays an important role in maintaining oral health.(Botelho, Machado, Proença, Delgado, & Mendes, 2020).

As we know, vitamin D is produced from the provitamin ergosterol in plants and 7-dehydrocholesterol in animals and humans.In humans, direct exposure to ultraviolet B/UVB rays can convert 7-dehydrocholesterol into cholecalciferol, which will then become vitamin D. (Hall, 2015; L.Z. Sherwood, 2016). Through the hydroxylation process in the liver and kidneys, the final product will be 1.25 hydroxyl cholecalciferol and 24.25 hydroxyl cholecalciferol(Rodwell, Bender, Botham, Kennelly, & Weil, 2015). If true, vitamin D is able to prevent the incidence of hypercholesterolemia, the incidence of hypercholesterolemia should not increase as it is today, as we know Indonesia is located in the equatorial area which gets continuous sun exposure throughout the year.

However, many studies have also reported the occurrence of problems with vitamin D deficiency in the blood.In fact, the problem of vitamin D deficiency in the blood has become a health problem in many countries and has become a global pandemic (Michael F Holick, 2017). Data shows that about 40% of the population in Europe have a vitamin D deficiency (Cashman et al., 2016). In fact, vitamin D deficiency also occurs in populations living in tropical countries, where it is possible to be exposed to the sun continuously, such as in Southeast Asia and Brazil (Hataikarn Nimitphong & Michael F.Holick, 2013; Mendes, Hart, Botelho, & Lanham-New, 2018). Several studies have reported that many populations experience vitamin D deficiency in all age groups, but the incidence will increase in children and in the elderly (Kevin D. Cashman, 2020).

This condition has attracted the authors to investigate more deeply and analyze the relationship between blood vitamin D levels and the incidence of hypercholesterolemia. The purpose of this study was to analyze blood vitamin D levels in students of the Faculty of Medicine class 2017 Malahayati University Bandar Lampung who suffered from hypercholesterolemia.

METHOD

This study is an analysis survey study with a case control approach that studies and analyzes the relationship between blood vitamin D levels and total cholesterol levels in hypercholesterolemic patients.

Participant characteristics and research design

The population of this study were students of the Faculty of Medicine, Malahayati University class of 2017 who suffered from hypercholesterolemia. The case samples in this study were the total medical faculty students whose cholesterol levels were above 200 mg/dL (hypercholesterolemia). The students who suffer from hypercholesterolemia are 26 people. Meanwhile, the control/comparison samples were medical school students who had normal total cholesterol levels (below 200 mg/dL) as many as 26 people,so that the total number of research samples was 52 people with a comparable ratio of case and control samples was 1 to 1.The sampling technique used in this research is purposive sampling.

Sampling procedures

The procedure for taking research subjects begins with an initial selection to find the case group subjects who suffer from hypercholesterolemia, by examining total cholesterol levels in the population.After examining cholesterol levels in the student population, it was found that there were 26 subjects who had hypercholesterolemia (above 200 mg/dL),then proceed with taking subjects for the control group, while the number is the same as the number of subjects in the case group, so that the total subjects in this study amounted to 52 students.

After getting the research subjects, both cases and controls, then proceed with the measurement of the independent variables in this study, including: measurement of BMI, measurement of blood vitamin D levels, measurement of waist circumference, and continued with interviews to obtain data related to the amount of pocket

money, regular exercise, physical activity and patterns of indoor or outdoor activities.

Measures and covariates

The variable measured in this study was the total cholesterol level by directly checking the total cholesterol level of the research subjects using the Easy Touch GCU Multi Function Monitor System Model ET-201.

The variable also measured in this study was blood vitamin D levels by measuring blood levels of 25(OH)D3. The method of measuring levels of 25(OH)D3 using the Direct competitive chemilumine scence immunoassay (CLIA) method, using Liaison 25-OH Vitamin D reagent for total production from DiaSorin Liaison with catalog number 310600.This method will be able to detect levels of 25(OH)D3 between 4 and 150 ng/mL.For examination of 25(OH)D3 levels, 5 cc of blood samples was taken in the morning, at which night fasting was recommended. The blood was centrifuged at a speed of 1300-2000 g for 15 minutes, then separated the serum and put it in a device for examination at the Prodia Clinical Laboratory, Lampung Province.

The variable that was also measured in this study was Body Mass Index (BMI) by measuring the sample's height and weight and measuring the subject's waist circumference. BMI measurement is carried out directly by measuring the sample's height and weight, then input into the BMI formula to calculate the BMI. Measurement of the subject's height was carried out using a GEA 26SM height meter which was placed on a flat wall with a height of 2 meters/200 cm.the subject was first asked to remove footwear, then asked to stand straight under the height measuring device.The position of the subject standing upright with his back against the wall and the subject's face straight ahead, then his height

was measured.Meanwhile, body weight was measured in the morning before breakfast using a digital BB scale GEA Medical Model BR9807 with a sensitivity of one digit behind the comma.Body weight measurements were repeated 2 times. This is done to ensure getting the correct weight.

Measurement of waist circumference using a tape measure, first make sure that the subject's clothing does not interfere with the measurement. The research subject stood upright and the tape measure was wrapped around the subject's abdomen and aligned/parallel to the belly navel. The tape measure is tightened, neither too tight nor too loose and make sure the subject is not holding his breath while the measurement is taking place.The waist circumference standard used in this study is the standard waist circumference measurement for Asians according to WHO (Alberti, Zimmet, & Shaw, 2006).

Meanwhile, for the gender variable, the amount of pocket money, the regularity of exercise and the pattern of indoor or outdoor activities, this is done by direct interviews with research subjects using a list of questions that have been prepared.

All study variables were measured once for each group (cases and controls). All of these research steps have taken into account the principles of research ethics and have received an ethical clearance letter by letter no. 1112/EC/KEP-UNMAL/III/2020 from the Health Research Ethics Commission of Malahayati University.

Data analysis

Data related to gender, body mass index (BMI), waist circumference, pocket money, blood vitamin D levels, exercise regularly, activity patterns and total cholesterol levels were tabulated and analyzed using the chi square test.

RESULTS AND DISCUSSION

Tabel 1.
Descriptive data

Variabel	Case			Control		
	Mean	+SD	Min-Max	Mean	+SD	Min-Max
Cholesterol Levels(mg/dL)	215,8	17,4	200-253	155,4	24,6	101-189
Blood vit D Levels(ng/dL)	12,6	3,9	8-22	17,8	5,4	10-34
BMI(kg/m^2)	27,7	5,7	18-41	23,8	5,9	19-39
waistCircumference(cm)	88,1	13,4	63-110	78,7	12,2	65-106

In table 1, it can be seen that the average cholesterol level in the case group was 215.8 + 17.4 with a minimum value of 200 mg/dL and the highest value of 253 mg/dL. Meanwhile, the average total cholesterol level in the control group was much lower: 155.4 + 24.6 with a minimum value of 101 mg/dL and the highest value of 189 mg/dL.The blood vitamin D levels in the case group were 12.6 + 3.9 with a minimum value of 8 ng/dL and a maximum value of 22 ng/dL. Meanwhile, the average blood vitamin D level in the control group was slightly higher: 17.8 + 5.4 with a minimum value of 19 ng/dL and a maximum value of 34 ng/dL.The average BMI in the case group was 27.7 + 5.7 with a minimum value of 18 kg/m2 and a maximum of 41 kg/m2. While the average BMI in the control group was lower: 23.8 + 5.9, with a minimum value of 19 kg/m2 and a maximum of 39 kg/m2. The average waist circumference in the case group was 88.1 + 13.4 cm with a minimum value of 63 cm and a maximum of 110 cm. Meanwhile, the average waist circumference in

the control group was smaller: 78.7 + 12.2 cm with a minimum value of 65 cm and a maximum value of 106 cm.

From table 2, it can be seen that both in the case group and in the control group, most of them had blood vitamin D levels in the very low category (below 10 ng/dL) and there was only one sample in the case group that had sufficient vitamin D levels. Statistical test results show that there is a significant relationship between blood vitamin D levels and blood cholesterol levels (pValue 0.005), with an OR value of 3.4, this indicates that people who have very low levels of vitamin D are at risk for an increase in cholesterol levels of 3.4 times when compared to people who have blood levels of vitamin D in the sufficient category.

The low blood levels of vitamin D in almost all of the samples in this study confirmed the initial hypothesis that widespread vitamin D deficiency had resulted in a global pandemic (Michael F Holick, 2017). Not only in countries with four seasons, but also occurs in populations living in

tropical areas that are rich in sunlight. Changes in behavior to avoid sunlight and patterns of activity in the room are thought to have contributed to this incident.

If it is associated with cholesterol levels, the results of this study support with studies reporting that vitamin D deficiency in the blood is associated with dyslipidemia. Levels of 25(OH)D3 were inversely correlated with levels of LDL cholesterol and triglycerides, and positively correlated with levels of HDL cholesterol.(Jiang et al., 2019).Whereas an increase in LDL can have a negative effect on health, because LDL is often known as bad fat which contributes to an increase in some cases of non-communicable diseases (Baghbani-Oskouei et al., 2018). The results of this study are also corroborated by studies that report that taking

cholesterol-lowering drugs can reduce blood vitamin D levels, so long-term use can affect bone health. Therefore, taking supplements and foods rich in vitamin D while taking cholesterol-lowering drugs is highly recommended. (Taefehshokr, Taefehshokr, & Key, 2019).

Vitamin D is believed to be able to reduce body fat by increasing insulin sensitivity and reducing parathyroid hormone levels, both of which will reduce hunger and increase fat disposal in the feces and decrease lipogenesis. (Vanlint, 2013). Low parathyroid hormone will cause blood calcium to increase which will be followed by an increase in sympathetic nerve activity, which will increase body heat. This condition causes an increase in the destruction of body fat in people who have normal blood levels of vitamin D.

Tabel 2.
Analisis bivariate

	Hypercholesterol (above 200 mg/dL)	Normal Cholesterol (below 200 mg/dL)	p value	OR (CI: 95%)
Very low vitamin D (below 10 ng/dL)	25	17	0.005	3.4 (1.5-11.4)
Very lacking / sufficient Vit D (10 -30mg/dL)	1	9		
Obesity (BMI$\geq$ 25kg/m^2)	20	5	0.001	4.0 (2.6-14.2)
Normal (BMI< 25kg/m^2)	6	21		
Abnormal waist circumference	20	10	0.005	5.3 (2.5 – 11.8)
Normal waist circumference	6	16		
Extra pocket money (more than the provincial minimum wage)	14	13	0.788	
Enough pocket money (below the provincial minimum wage)	12	13		
Irregular exercise (less than 3 times/week)	22	14	0.016	4.7 (1.2-11.5)
Regular exercise (3 times per week)	4	12		
Active indoors	25	14	0.001	5.1 (2.1 -18.2)
Active outdoors	1	12		
Female	18	16	0.560	
Male	8	10		

From table 2, it can be seen that most of the case groups are obese people with BMI above 25 kg/m2 and conversely in the control group most of them are people who have normal weight/normal BMI.Statistical tests also showed a significant relationship (pValue: 0.001) between body weight (BMI) and increased cholesterol levels with an OR value of 4.0. This means that people who are obese are 4 times more likely to suffer from hypercholesterolemia, when compared to people who have normal weight.

These results are corroborated by studies in children in Negeria who reported a correlation between cholesterol levels and BMI, so that an increase in BMI was used as an early indicator of hypercholesterolemia in children. (Nwaiwu & Ibe, 2015). However, with increasing age, the relationship between cholesterol levels and BMI becomes weak or unclear (Laclaustra et al., 2018), This shows that weight loss in old age is not necessarily followed by a decrease in blood cholesterol levels.

The data in table 2 shows that most of the waist circumference in the case group is excessive, while in the control group most of the waist circumference is in the normal category. Statistical tests also showed a significant relationship between waist circumference and hypercholesterolemia with an OR value of 5.3, which means that people who have excess waist circumference will have a 5.3 times risk of developing hypercholesterolemia when compared to those who have normal waist circumference. These results support the results of a study which reported

that there was a relationship between a decrease in waist circumference and weight loss, which was also influenced by gender.(Rothberg et al., 2017). Women are more likely to have a larger waist circumference than men. Women are influenced by sex hormones such as estrogen which affect fat metabolism in the body, so women will tend to accumulate fat at reproductive age.However, the opposite results were reported that studies in menopausal women reported that there was an effect of reduced estrogen on increasing obesity in postmenopausal women, so it is necessary to consider giving estrogen therapy to obese menopausal women. (Lizcano & Guzmán, 2014).

Table 2 also shows that exercise is associated with cholesterol levels with a pValue (0.016) and an OR value of 4.7. This means that people who do not regularly exercise (3 times / week) will be at risk of suffering from an increase in cholesterol levels 4.7 times when compared to people who regularly exercise (3 times / week).

Exercise has been believed to be able to lose weight and can also have a positive effect on a person's physical and mental health. Exercise will accelerate blood circulation and burn excess calories in the body (Hermawan et al., 2020). Regular exercise will not only lose weight but also has many other benefits such as a healthy heart, breathing, and strengthening muscles and bones.(Garber, 2019).Exercise is believed to be the most appropriate choice for lowering blood cholesterol levels so that a person does not always depend on cholesterol-lowering drugs (Wang & Xu, 2017).

The more a person exercises regularly, the better for his health, especially if the exercise is done outdoors so that the skin is exposed to the sun.(Hermawan, 2021), so that the process of vitamin D biosynthesis in the skin can occur optimally.

Table 2 also shows that the habit of indoor activities is also associated with hypercholesterolemia with a p-value of 0.001 and an OR value of 5.1. This means that people who are usually active indoors have a 5.1 times risk of suffering from hypercholesterolemia when compared to those whose daily activities are outdoors.Being active outdoors will be able to make a person active so that more calories will be used to produce energy when compared to people who are active indoors.People who are active indoors tend to be limited in their movements so that a lot of energy reserves are converted into fat deposits under the skin. Another reason, is that people who are more active indoors, are less likely to be exposed to ultraviolet B/UVB rays from sunlight, which are necessary for the biosynthesis of pro-vitamin D into vitamin D.(Hall, 2015). Even though it is known that vitamin D is associated with an increase in cholesterol/body fat levels, this even occurs in people who are not obese(Kim & Jeong, 2019).This explains the strong relationship between blood vitamin D levels and blood cholesterol levels without being affected by an increase or decrease in body weight.

Meanwhile, the amount of pocket money and gender are not related to cholesterol levels. In general, pocket money is associated with the habit of consuming unhealthy snacks/foods in children, which will have an effect on increasing weight/obesity.(Li et al., 2017). In this study, because the subjects were late teens, who were medical students with better health knowledge, this condition was thought to lead to wiser use of pocket money. So even though the pocket money is excessive, it doesn't cause them to consume unhealthy snacks, so the pocket money is not related to the incidence of hypercholesterolemia.

Likewise with gender, although the data show that more women have hypercholesterolemia, there is no statistically significant relationship between gender and hypercholesterolemia.In female subjects of reproductive age, sex hormones, such as estrogen, are thought to be responsible for weight gain in women at this age.Estrogen shows different effects on women of reproductive age and menopausal age. In women of reproductive age, an increase in estrogen is thought to cause weight gain, while in women who experience menopause, a very low decrease in estrogen during menopause is thought to be associated with an increase in obesity cases at that time.(Lizcano & Guzmán, 2014).Meanwhile, male subjects will be influenced by the hormone testosterone which affects muscle mass by increasing muscle protein synthesis.(Gharahdaghi et al., 2021), So both men and women in the reproductive period, sex hormones can affect weight gain and will also have an effect on cholesterol/blood fat levels. This reason is thought to cause gender not to be significantly related to cholesterol levels in this study.

LIMITATION OF THE STUDY

In this study, cholesterol measurements used a simple measurement tool: Easy Touch GCU Multi Function Monitor System, so there may be inaccuracies related to the total cholesterol level data taken.

CONCLUSIONS AND SUGGESTIONS

There is a significant relationship between blood vitamin D levels and total cholesterol levels, the lower the blood vitamin D levels, the higher the cholesterol levels. Increased body weight, waist circumference, regular exercise and outdoor activity habits were also significantly associated with blood cholesterol levels.

To maintain blood cholesterol levels in normal conditions, it is necessary to maintain vitamin D levels in the blood, through increasing consumption of foods containing vitamin D and by increasing activities and outdoor sports to get UVB rays exposure from sunlight.

REFERENCES

Alberti, K. G. M. M., Zimmet, P., & Shaw, J. (2006). Metabolic syndrome - A new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabetic Medicine*, *23*(5), 469–480. https://doi.org/10.1111/j.1464-5491.2006.01858.x

Baghbani-Oskouei, A., Tohidi, M., Asgari, S., Ramezankhani, A., Azizi, F., & Hadaegh, F. (2018). Serum lipids during 20 years in the Tehran lipid and glucose study: Prevalence, trends and impact on non-communicable diseases. *International Journal of Endocrinology and Metabolism*, *16*(4). https://doi.org/10.5812/ijem.84750

Besseling, J., Kastelein, J. J. P., Defesche, J. C., Hutten, B. A., & Hovingh, G. K. (2015). Association between familial hypercholesterolemia and prevalence of type 2 diabetes mellitus. *JAMA - Journal of the American Medical Association*, *313*(10), 1029–1036. https://doi.org/10.1001/jama.2015.1206

Botelho, J., Machado, V., Proença, L., Delgado, A. S., & Mendes, J. J. (2020). Vitamin D deficiency and oral health: A comprehensive review. *Nutrients*, *12*(5). https://doi.org/10.3390/nu12051471

Cashman, K. D., Dowling, K. G., škrabáková, Z., Gonzalez-Gross, M., Valtueña, J., De Henauw, S., … Kiely, M. (2016). Vitamin D deficiency in Europe: Pandemic? *American Journal of Clinical Nutrition*, *103*(4), 1033–1044. https://doi.org/10.3945/ajcn.115.120873

Garber, C. E. (2019). The Health Benefits of Exercise in Overweight and Obese Patients. *Current Sports Medicine Reports*, *18*(8), 287–291. https://doi.org/10.1249/JSR.0000000000000619

Gharahdaghi, N., Phillips, B. E., Szewczyk, N. J., Smith, K., Wilkinson, D. J., & Atherton, P. J. (2021). Links Between Testosterone, Oestrogen, and the Growth Hormone/Insulin-Like Growth Factor Axis and Resistance Exercise Muscle Adaptations. *Frontiers in Physiology*, *11*(January), 1–12. https://doi.org/10.3389/fphys.2020.621226

Gibbs, A. (2018). *Lowering Cholesterol: Simple Lifestyle Changes to Lower Cholesterol Naturally and Prevent Heart Disease - PDFDrive.com*. Angela Gibbs.

Hall, J. E. (2015). *Guyton and Hall review physiology* (13th ed.). Philadelphia: Sauders-Elsevier.

Hataikarn Nimitphong, & Michael F.Holick. (2013). Prevalence of Vitamin D Deficiency in Asia Vitamin D status and sun exposure in Southeast Asia. *Dermato-Endocrinology*, *5*(1), 34–37.

Heart Association, A. (2018). *Cholesterol Management Guide www.heart.org/cholesterol FOR HEALTHCARE PRACTITIONERS Cholesterol Management Guide*.

Hermawan, D. (2021). *Manfaat Vitamin D pada Era Pandemi Covid-19*. Yogyakarta, Indonesia: Penerbit Buku Andi. Retrieved from https://books.google.co.id/books?id=kNA3EAAAQBAJ&printsec=frontcover&hl=id&source=gbs_ge_summary_r&cad=0#v=onepage&q&f=false

Hermawan, D., Muhani, N., Sari, N., Arisandi, S., Widodo, S., Lubis, M. Y., … Firdaus, A. A. (2020). *Mengenal Obesitas*. Yogyakarta: Penerbit Buku Andi. Retrieved from https://books.google.co.id/books?id=mY_5DwAAQBAJ&printsec=frontcover&hl=id&source=gbs_atb#v=onepage&q&f=false

Hubková, B., Bódy, G., Mašlankováa, J., Birková, A., Frišman, E., Kraus, V., & Mareková, M. (2018). Lipoprotein-cholesterol fractions in marginalized Roma versus majority population. *International Journal of Environmental Research and Public Health*, *15*(1). https://doi.org/10.3390/ijerph15010081

Jiang, X., Peng, M., Chen, S., Wu, S., & Zhang, W. (2019). Vitamin D deficiency is associated with dyslipidemia: a cross-sectional study in 3788 subjects. *Curr Med Res Opin*, *35*(6), 1059–1063.

Kementrian Kesehatan Republik Indonesia. (2018). *Riskesdas 2018*. Jakarta, Indonesia: Sekretariat Litbang Kesehatan Kemenkes.

Kevin D. Cashman. (2020). Vitamin D Deficiency: Defining, Prevalence, Causes, and Strategies of Addressing. *Calcif Tissue Int*, *106*, 14–29. https://doi.org/https://doi.org/10.1007/s00223-019-00559-4

Kim, M. R., & Jeong, S. J. (2019). Relationship between vitamin D level and lipid profile in non-obese children. *Metabolites*, *9*(7). https://doi.org/10.3390/metabo9070125

L.Z. Sherwood. (2016). *Human Physiology form cell to systems* (9th ed.). Boston: Cangage Learning.

Laclaustra, M., Lopez-Garcia, E., Civeira, F., Garcia-Esquinas, E., Graciani, A., Guallar-Castillon, P., … Rodriguez-Artalejo, F. (2018). LDL cholesterol rises with BMI only in lean individuals: Cross-sectional U.S. And Spanish representative data. *Diabetes Care*, *41*(10), 2195–2201. https://doi.org/10.2337/dc18-0372

Li, M., Xue, H., Jia, P., Zhao, Y., Wang, Z., Xu, F., & Wang, Y. (2017). Pocket money, eating behaviors, and weight status among Chinese children: The Childhood Obesity Study in China mega-cities. *Preventive Medicine*, *100*, 208–215. https://doi.org/https://doi.org/10.1016/j.ypmed.2017.04.031.

Lizcano, F., & Guzmán, G. (2014). Estrogen deficiency and the origin of obesity during menopause. *BioMed Research International*, *2014*. https://doi.org/10.1155/2014/757461

Mendes, M. M., Hart, K. H., Botelho, P. B., & Lanham-New, S. A. (2018). Vitamin D status in the tropics: Is sunlight exposure the main determinant? *Nutrition Bulletin*, *43*(4), 428–434. https://doi.org/10.1111/nbu.12349

Michael F Holick. (2017). The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. *Rev Endocr Metab Disord*, *18*(2), 153–165. https://doi.org/0.1007/s11154-017-9424-1

Mosca, A., Strologo, A. Dello, Sanseviero, M., Serena, M., Alterio, T., Zaffina, S., & Nobili, V. (2019). Vitamin D deficiency is associated with high levels of LDL cholesterol in NAFL children, *4*, 1–5. https://doi.org/10.15761/GIMCI.1000175

Navar-Boggan, A. M., Peterson, E. D., D'Agostino, R. B., Neely, B., Sniderman, A. D., & Pencina, M. J. (2015). Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease. *Circulation*, *131*(5), 451–458. https://doi.org/10.1161/CIRCULATIONAHA.114.012477

Nwaiwu, O., & Ibe, B. C. (2015). Relationship between serum cholesterol and body mass index in Nigeria schoolchildren aged 2-15 years. *Journal of Tropical Pediatrics*, *61*(2), 126–130. https://doi.org/10.1093/tropej/fmu080

Rao, W., Su, Y., Yang, G., Ma, Y., Liu, R., Zhang, S., … Yu, Q. (2016). Cross-sectional associations between body mass index and hyperlipidemia among adults in northeastern China. *International Journal of Environmental Research and Public Health*, *13*(5). https://doi.org/10.3390/ijerph13050516

Rodwell, V. W., Bender, D. A., Botham, K. M., Kennelly, P. J., & Weil, P. A. (2015). *Harper's illustrated biochemistry* (30th ed.). New York: Mcgraw-Hill Education.

Rothberg, A. E., McEwen, L. N., Kraftson, A. T., Ajluni, N., Fowler, C. E., Nay, C. K., … Herman, W. H. (2017). Impact of weight loss on waist circumference and the components of the metabolic syndrome. *BMJ Open Diabetes Research and Care*, *5*(1), 3–8. https://doi.org/10.1136/bmjdrc-2016-000341

Sarkar, A., & Roy, D. (2017). Is vitamin D deficiency contributing to high predisposition to non-communicable diseases in Indians? A review article. *International Journal Of Community Medicine And Public Health*, *4*(8), 2637. https://doi.org/10.18203/2394-6040.ijcmph20173307

Taefehshokr, S., Taefehshokr, N., & Key, Y. A. (2019). The effects of cholesterol lowering drugs on vitamin D status in familial hypercholesterolemia patients. *Archives of Medical Laboratory Sciences*, *3*(4), 3–8. https://doi.org/10.22037/amls.v3i4.19099

Vanlint, S. (2013). Vitamin D and obesity. *Nutrients*, *5*(3), 949–956. https://doi.org/10.3390/nu5030949

Wang, Y., & Xu, D. (2017). Effects of aerobic exercise on lipids and lipoproteins. *Lipids in Health and Disease*, *16*(1), 1–8. https://doi.org/10.1186/s12944-017-0515-5