Jurnal Kedokteran dan Kesehatan Indonesia

Indonesian Journal of Medicine and Health

Journal homepage: https://journal.uii.ac.id/JKKI

JKKI
SCIENTIA EST BASIC VITAE

Association between melanin and vitamin D: A systematic review

Andre Colin Hartono[1], Veronika Maria Sidharta[2], Yunisa Astiarani[3], Regina Regina*[4]

[1]Bachelor of Medicine Study Programme, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia
[2]Department of Histology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia
[3]Department of Public Health and Nutrition, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia
[4]Department of Dermatology and Venereology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

Literature Review

ARTICLE INFO

Keywords:
melanin,
vitamin D,
skin pigment,
photoprotective

***Corresponding author:**
regina@atmajaya.ac.id

DOI: 10.20885/JKKI.Vol14.Iss1.art13

History:
Received: January 12, 2022
Accepted: February 5, 2023
Online: April 5, 2023

ABSTRACT

Globally, there is an increasing prevalence of vitamin D deficiency, including in Southeast Asia, which ranges from 6% to 70%. Vitamin D plays an important role in calcium metabolism and bone health. Melanin is one factor that contributes to vitamin D deficiency. It has photoprotective properties that inhibit vitamin D synthesis, but the mechanism has not been fully understood. To determine the mechanism of the association between melanin and vitamin D, this systematic review was conducted on 11 articles, including cross-sectional studies, cohort studies, and randomised controlled trials published from 2010 to 2020. The search included Pubmed, EBSCO, and Proquest databases, and data were synthesised from 11 studies. This critical review found nine of the 11 studies reported a significant association between melanin and vitamin D, while two reported non-significant results. Of the nine significant studies, eight reported that people with higher melanin have lower vitamin D levels, while one study suggested that melanin levels do not necessarily associate with lower vitamin D levels. In conclusion, the review establishes a significant association between melanin and vitamin D.

Secara global, prevalensi defisiensi vitamin D cenderung meningkat, termasuk di Asia Tenggara yang berkisar antara 6% hingga 70%. Vitamin D memiliki peran penting dalam metabolisme kalsium dan kesehatan tulang. Melanin adalah salah satu faktor yang berkontribusi terhadap kekurangan vitamin D. Melanin memiliki sifat fotoprotektif yang menghambat sintesis vitamin D, namun mekanisme ini belum sepenuhnya dipahami. Untuk menentukan mekanisme hubungan antara melanin dan vitamin D, dilakukan tinjauan sistematis pada 11 artikel, seperti studi potong-lintang, studi kohort, dan uji klinis acak yang diterbitkan dari tahun 2010 hingga 2020. Pencarian dilakukan pada database Pubmed, EBSCO, dan Proquest, dan data disintesis dari 11 studi. Tinjauan kritis ini menemukan bahwa sembilan dari 11 studi melaporkan adanya hubungan yang signifikan antara melanin dan vitamin D, sementara dua studi melaporkan hasil yang tidak signifikan. Dari sembilan studi yang signifikan, delapan melaporkan bahwa orang yang memiliki melanin lebih tinggi memiliki kadar vitamin D yang lebih rendah, sementara satu studi menyatakan bahwa kadar melanin tidak selalu berkaitan dengan rendahnya kadar vitamin D. Kesimpulannya, tinjauan ini menegaskan adanya hubungan yang signifikan antara melanin dan vitamin D.

INTRODUCTION

A previous study estimated that around 1 billion of the world's population is deficient in vitamin D, and about 50% have vitamin D insufficiency.[1] In Indonesia, there is no actual prevalence rate of vitamin D deficiency, but a study by South East Asian Nutrition Surveys (SEANUTS) in 2016, reported that 5.6% of respondents in Indonesia had a desirable vitamin D level.[2] Another study in Jakarta demonstrated that the incidence of vitamin D deficiency in women aged 45-55 years reached 50%.[3] Studies on elementary school students in Jakarta reported an alarming insufficiency rate (75.9%), of which 15% were deficient.[4] Based on the endocrine association, a study by Aji et al. on pregnant women in the Minangkabau area gave a figure of 36.2% for severe deficiency and 46.6% for deficiency.[5] Further, Vitamin D deficiency was detected in 90% of cord blood samples (birth) and 13% of venous blood samples at six months of age in Yogyakarta, Indonesia.[6]

According to the Institute of Medicine, vitamin D deficiency is a condition when the level of 25-hydroxyvitamin D (25(OH)D) in the serum is less than 30 nmol/L and sufficient if 25(OH)D is more than 50 nmol/L.[7] Vitamin D is important in calcium metabolism, bone health, and muscle function.[8,9]

Vitamin D deficiency has been strongly associated with various health outcomes, including all-cause mortality.[10] Vitamin D deficiency results from a variety of factors and conditions. These include a lack of vitamin D consumption in the diet, as well as a reduction in vitamin D absorption caused by certain conditions like celiac disease, inflammatory bowel disease, short bowel syndrome, chronic pancreatitis, and cystic fibrosis. Other contributing factors include liver cirrhosis, kidney failure, and the use of drugs such as phenobarbital, carbamazepine, dexamethasone, nifedipine, spironolactone, clotrimazole, and rifampin, as these medications can stimulate hepatic p450 enzymes and accelerate vitamin D catabolism. Additionally, lack of exposure to sunlight can result in insufficient vitamin D synthesis.[11]

Furthermore, recent studies have reported an association between age and skin pigment concerning vitamin D synthesis. Specifically, as a person ages, their ability to synthesise vitamin D decreases. Similarly, individuals with high levels of skin pigments, such as melanin, tend to have slower rates of vitamin D synthesis.[11–13] Melanin has photoprotective properties that can protect the body from ultraviolet radiation (UVR), so the amount of melanin is thought to affect the skin's ability to synthesise vitamin D.[14] However, the mechanism has not been fully understood. A study by Young et al. on 102 volunteers with varying levels of Fitzpatrick skin type revealed a very small association between melanin and Vitamin D synthesis.[15]

Due to the inconsistent results of previous studies, the present study aimed to critically evaluate the association between melanin and vitamin D levels across all age groups, to understand the mechanism of melanin in the biosynthesis of vitamin D, and provide valuable evidence for future studies.

This study utilised a systematic review, following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) flow diagram, which involved several stages (Figure 1). Articles were retrieved from three databases, including PubMed, EBSCO, and ProQuest, using a combination of the keywords vitamin D and melanin. To refine the selection of articles, duplicate keywords were eliminated using the Zotero program, and inclusion and exclusion criteria were applied. The inclusion criteria were articles published in English or Bahasa Indonesia between 2010 and 2020, which involved a sample population of all age groups and employed cross-sectional studies, cohort studies, or randomised controlled trials. Conversely, the exclusion criteria comprised articles that were not full-text or whose study respondents had a vitamin D metabolism disorder.[17,18] Selected articles were summarised in a table, including the first author, published year, location, study design, vitamin D analysis method, melanin analysis method, number of respondents, mean of vitamin D level, and results (Tables 1 and 2).

The quality of the article was assessed using the Newcastle Ottawa Assessment Scale (NOS) and The Joanna Briggs Institute (JBI).[19,20] After being extracted and assessed for quality, the article was analysed and interpreted to obtain evidence for the conclusion.

The role of melanin in the biosynthesis of vitamin D

Melanocytes found around 12.2-12.8 melanocytes/mm in adult human epidermis, consistent regardless of light or dark skin. Melanocytes are a slow-dividing cell type with a proliferation rate of less than twice per year, allowing them to stay at the basal layer of the epidermis. UV exposure gives keratinocytes in epidermal signal to activate p53 mediated expression of proopiomelanocortin (POMC), which upon post-translational cleavage generates a paracrine factor, α melanocyte-stimulating

Table 1. Demographic characteristics article on the association of melanin and vitamin D

No	Authors	Title	Objective	Conclusion
1.	Laura M. Hall, et al.[21]	Vitamin D intake needed to maintain target serum 25-hydroxyvitamin D concentrations in participants with low sun exposure and dark skin pigmentation is substantially higher than current recommendations	Make quantitative assessments to predict vitamin D status based on sun exposure and skin pigment	Participants with high skin reflectance and high sun exposure had a small risk of vitamin D insufficiency, whereas participants with low skin reflectance and low sun exposure tended to have a greater risk
2.	Jacqueline Chan, et al.[22]	Determinants of serum 25 hydroxyvitamin D levels in a nationwide cohort of blacks and non-Hispanic whites	Develop predictive equations on s25(OH) D levels with large populations and diverse races	Age and sun exposure affect s25(OH)D levels differently in blacks and whites
3.	Mark D Farrar, et al.[23]	Recommended summer sunlight exposure amounts fail to produce sufficient vitamin D status in UK adults of South Asian origin	To determine the effect of UVR exposure on Asian and white skin pigments on vitamin D status	The effect of UVR exposure is not significant to affect vitamin D status
4.	Adam B. Murphy, MD, MBA, et al.[24]	Predictors of Serum Vitamin D Levels in African American and European American Men in Chicago	Knowing three factors that can affect vitamin D levels in African-American	Factors of vitamin D supplementation and sun exposure were significant in maintaining vitamin D levels in both races
5.	Marcelo Azevedo Cabral, et al.[29]	Prevalence of vitamin D deficiency during the summer and its relationship with sun exposure and skin phototype in elderly men living in the tropics	Knowing the prevalence of vitamin D deficiency in older men and its relationship with sun exposure and skin type	The prevalence of vitamin D deficiency in older men is high in the tropics
6.	Lauren E. Au, et al.[25]	Association of serum 25-hydroxyvitamin D with race/ ethnicity and constitutive skin colour in urban schoolchildren	Knowing the reason skin colour affects differences in vitamin D levels in certain races/ethnicities	Race/ethnicity and skin colour have a relationship with serum vitamin D levels
7.	Tim J. Green, et al.[26]	Vitamin D supplementation is associated with higher serum 25OHD in Asian and White infants living in Vancouver, Canada	Knowing the 25(OH)D concentration in children of Asian ethnicity and white people living in Canada	The children of the study were highly protected against rickets (vitamin D concentration < 10ng/mL)
8.	Kumaravel Rajakumar, et al.[27]	Estimations of dietary vitamin d requirements in black and white children	Knowing the need for vitamin D intake in children to achieve the recommendations of the IOM	The concentration of 25(OH) D is influenced by vitamin D intake, which should be adjusted based on pubertal status.
9.	Clare F. Dix, et al.[30]	Association of Sun Exposure, Skin Colour and Body Mass Index with Vitamin D Status in Individuals Who Are Morbidly Obese	Identify factors that may affect vitamin D status in obese individuals	Individuals who are obese and have light natural skin colour may be at a higher risk for vitamin D insufficiency.
10.	Inger Ohlund, et al.[28]	Increased vitamin D intake differentiated according to skin colour is needed to meet requirements in young Swedish children during winter: a double-blind, randomised clinical trial	Evaluate the amount of vitamin D needed to maintain an adequate 25(OH)D concentration	Children with white or black-pigmented skin need vitamin D supplements to maintain 25(OH)D concentrations
11.	Antony R. Young, et al.[15]	Melanin has a Small Inhibitory Effect on Cutaneous Vitamin D Synthesis: A Comparison of Extreme Phenotypes	Knowing the effect of Fitzpatrick Skin Type and ethnicity on the formation of vitamin D from sun exposure	Melanin inhibits the production of vitamin D

Table 2. Demographic characteristics article on the association of melanin and vitamin D

No	Authors	Year	Location	Study Design	Vitamin D Analysis Method	Melanin Analysis Method	Mean/Median	Number of Respondents (Age)	Vitamin D Mean (ng/mL)	Result
1.	Laura M. Hall, et al.[21]	2010	US	Cohort Study	RIA, LC-MS/MS	Spectrophotometer	African 44 ± 7 L*; South Asian 54 ± 5 L*; Hispanic 58 ± 4 L*; North Asian 59 ± 4 L*; European 63 ± 4 L*	72 (19-39)	17.2-26.4	Significant+
2.	Jacqueline Chan, et al.[22]	2010	US	Cohort Study	RIA	FST	-	209 + 236 (58-63)	20-30.8	Significant+
3.	Mark D Farrar, et al.[23]	2011	England	Cohort Study	HPLC	Spectrophotometer	South Asian, 41.11 ± 12.84 L*	15 (20-60)	5.8-14.8	Significant+
4.	Adam B. Murphy, MD, MBA, et al.[24]	2012	US	Cross-sectional Study	CLIA	Narrow-band reflectometer	-	558 (40-79)	21	Significant+
5.	Marcelo Azevedo Cabral, et al.[29]	2013	Brazil	Cross-sectional Study	ECLIA	FST	-	284 (> 60)	27.86	Not Significant-
6.	Lauren E. Au, et al.[25]	2014	US	RCT	LC-MS/MS	Reflectance Colorimetry	ITAC° White 50.1°; Black -10.7° ; Hispanic/Latino 34.1°; Asian 28.7°; Multi-racial/other 31.3°; ITAF° White 28.6°; Black -28.0°; Hispanic/Latino 12.0°; Asian 9.1°; Multi-racial/other 11.8°	307 (11.4)	< 20	Significant+
7.	Tim J. Green, et al.[26]	2015	Canada	Cross-sectional Study	CLIA	Spectrophotometer	ITA° 50.6°	65 (2-4 months)	31	Significant+
8.	Kumaravel Rajakumar, et al.[27]	2016	US	RCT	LC-MS/MS	Dermatospectrophotometer	Median: 49.9 (36.2-67.9)	96 (8-14)	17; 23.4	Significant+
9.	Clare F. Dix, et al.[30]	2017	Australia	Cross-sectional Study	CLIA	Spectrophotometer	ITAC° 50.2° ± 8.2; ITAF° 26.6° ± 11.7	50 (23-61)	9.2-41.2	Not Significant-
10.	Inger Ohlund, et al.[28]	2017	Swedia	RCT	LC-MS/MS	FST	-	189 (5-7)	20	Significant+
11.	Antony R. Young, et al.[15]	2020	England	RCT	LC-MS/MS	Spectrophotometer	-	102 (20-29)	9 - 14.8	Significant+

RCT, Randomised Controlled Trials; RIA, Radioimmunoassay; LC-MS/MS, Liquid Chromatography Tandem Mass Spectrophotometry; HPLC, High-Performance Liquid Chromatography; CLIA, Chemiluminescence Immunoassay; ECLIA, Electro Chemiluminescent Competitive Immunoassay; FST, Fitzpatrick Skin Type ; + $p < 0,05$; - $p > 0,05$

hormone (α-MSH), which specifically binds to melanocortin 1 receptor (MC1R) found on the surface of melanocytes. Melanocytes then initiate cAMP-mediated melanin synthesis in cellular organelles called melanosomes, which carry the melanin to the epidermal keratinocytes.[31] The melanin pigment protects the underlying skin against damage from UVR. In reducing the UVR, it also reduces the vitamin D syntesis.[32]

The amount of melanin in the skin plays a crucial role in vitamin D production. Those with lighter skin, such as individuals with skin types I and II, have less melanin on the surface of their epidermis, allowing UV light to penetrate the skin and facilitate vitamin D biosynthesis. Consequently, they are capable of producing higher amounts of vitamin D. Conversely, individuals with darker skin, such as those with skin types V and VI, have higher levels of melanin on their epidermis, making it more difficult for UV light to penetrate and reach the site of vitamin D biosynthesis. This condition is due to the photoprotective effect of melanin, which reduces the amount of UV light that can penetrate the skin, resulting in reduced vitamin D production.[22]

Association between melanin and vitamin D

Nine of the 11 selected articles reported a significant ($p < 0.05$) association between melanin and vitamin D levels. These studies demonstrated a significant result regarding high vitamin D levels in people with lighter skin ($p < 0.05$).[15, 21–30] Hall et al. study demonstrated that people with lighter skin (high reflectance) had a lower risk of vitamin insufficiency D compared to people with darker skin (low reflectance).[21] Furthermore, Farrar et al. found similar findings that people with darker skin, even though exposed to sunlight, have the same results and do not increase vitamin D levels significantly.[23] Meanwhile, Cabral et al. reported an opposite finding, indicating no significant ($p > 0.05$) association between vitamin D status or levels in individuals with light or dark skin.[29] According to Dix et al. constitutive skin pigment was associated with vitamin D concentration ($p = 0.074$). However, there was no significant association between facultative skin pigment and vitamin D concentration.[30]

In the study conducted by Farrar et al. it was observed that exposure to UV light did not result in significant vitamin D production in dark-skinned individuals. This is because of their natural photoprotective mechanism, which reduces the penetration of UV rays into the epidermis. Dark-skinned individuals only absorb 7.4% UVB and 17.5% UVA, whereas light-skinned individuals can absorb 24% UVB and 55% UVA. Additionally, the biological process of melanin degradation through lysosomal enzymes is less effective in eumelanin, leading to higher levels of melanin and its photoprotective properties.

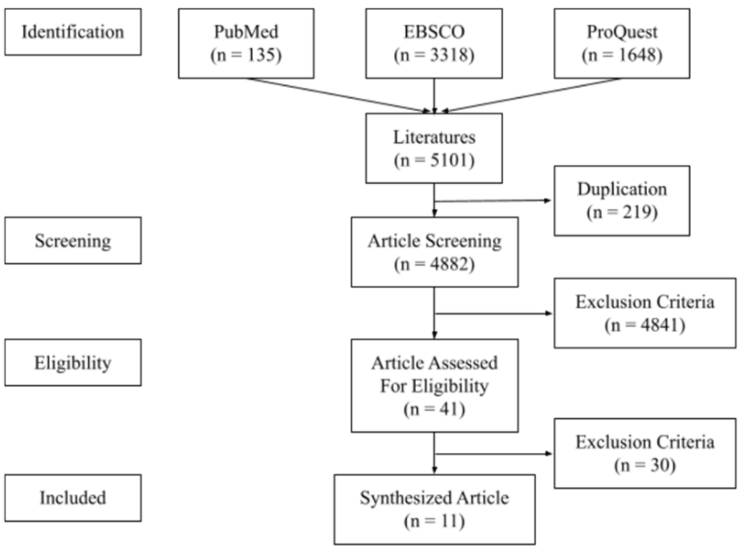

Figure 1. PRISMA Flow Diagram

Consequently, the exposure to UV rays that do penetrate is small, resulting in low vitamin D synthesis. However, any significant increase in vitamin D production will be short-lived because, after a week or more, the melanogenesis process causes an increase in melanin levels, leading to a decrease in UV penetration, and a reduction in vitamin D production.[23]

A previous study by Cabral et al. and Dix et al. reported different findings. Cabral et al. found no significant difference in vitamin D concentration between dark and light skin individuals (p = 0.46). However, it is important to note that the study by Cabral et al. had a small number of respondents with light skin (only 4 white individuals, 33 with dark skin, and the remainder with intermediate skin tones), which may have resulted in inaccurate comparative analysis.[29] Similarly, Dix et al. did not find a association between skin pigment and vitamin D concentration, possibly due to a limited number of respondents with dark skin, resulting in an insignificant comparison.[30]

Risk of bias

Regarding obtained cross-sectional studies, two articles with a moderate risk of bias at the selection stage, in which the samples from both articles did not represent the target population because they used convenience sampling at an institution and did not explain non-respondent bias.[26,29] Furthermore, two cohort studies have a moderate risk of bias because they choose respondents using convenience sampling, so they are not representative.[21,23] One cohort study also had a risk of bias at the comparability stage as it failed to control for important factors such as age, race, food/supplement intake, climate, and BMI.[22] The seven articles' outcome stages of cross-sectional and cohort studies had a low risk of bias.[21–24,26,29,30] Four studies using randomised controlled trials were included in the assessment.[15,25,27,28]

Factors influence vitamin D concentration

Vitamin D serum concentration is influenced by several factors, including race/ethnicity, which is closely related to skin colour. While it is believed that genetic differences affecting 7-dehydrocholesterol concentration or the conversion of vitamin D to 25(OH)D may not result in significant differences in the biosynthetic capacity of vitamin D, further research is required to establish evidence on this matter.[24]

A study by Laura et al. suggests that vitamin D intake alone does not significantly affect vitamin D serum concentration. However, adequate sun exposure could increase vitamin D serum concentration, particularly for light-skinned individuals.[22] It is important to note that people with dark skin have lower vitamin D serum production and, therefore, require greater vitamin D intake than those with light skin.[23]

As individuals age, their vitamin D serum levels may decrease slightly due to the decreased production of 7-dehydrocholesterol in the skin.[22,23] Additionally, a study found an inverse

Table 3. Assessment of article quality on cross-sectional studies of the association of melanin and vitamin D

Article	Selection				Comparability	Outcome		Total
First author, Year	Representative Sample	Sample	Non- Size Respondent	Ascertainment of the exposur	Factors are controlled	Assestment of the outcome	Statistical test	
Murphy, 2012	*	*	-	**	**	*	*	8
Cabral, 2013	-	*	-	*	**	*	*	6
Green, 2015	-	-	-	**	**	*	*	6
Dix, 2017	-	*	-	**	**	*	*	7

Very low risk of bias, points 9-10; Low risk of bias, points 7-8; Moderate risk of bias, points 5-6; High risk of bias, 0-4 points association between BMI and vitamin D serum concentration, with increasing weight or BMI leading to a decrease in vitamin D serum concentrations. However, this decrease is not significant. It is worth noting that vitamin D can be stored in adipose tissue, leading to a decrease in vitamin D concentration in the serum.[22]

According to Chan et al. the season significantly impacts changes in serum vitamin D levels compared to other factors, including sun exposure. The lowest vitamin D serum levels are observed during winter, while the highest levels are observed during summer. During the summer, UV strength peaks, leading to a cumulative effect where vitamin D remains stored when UVB strength is still high. This stored vitamin D is then released in the fall season.[23]

CONCLUSION

This systematic study examined 11 articles, with nine articles providing significant results regarding the association between melanin and vitamin D levels and two with non-significant results. There is no association between melanin and vitamin D levels. Of the nine articles, eight concluded that high levels of melanin in a person's skin or eumelanin have a high photoprotective effect, thereby inhibiting or reducing the production of vitamin D levels. One article reported that eumelanin and pheomelanin have no significant difference in inhibiting vitamin D production. This systematic study concluded that neither eumelanin nor pheomelanin was associated with vitamin D levels.

RECOMMENDATION

Most studies have used randomised controlled trials, but many have used other factors such as age, race, food/supplement, climate, cholesterol, and BMI. All of these factors can affect the results of the study. In addition, several cross-sectional and cohort studies could not explain the causal association in this study. Some studies also

Table 4. Assessment of the article quality of the cohort study of the association of melanin and vitamin D

Article	Selection				Comparability	Outcome			Total
First author, Year	Representative of Exposed Cohort	Non-Exposed Cohort	Ascertainment of the exposure	The outcome of interest was not present	Factors are controlled	Assessment of outcome	Follow-up outcome to occur	Adequacy of following up cohort	
Hall, 2010	-	-		*	**	*	*	*	7
Chan, 2010	*	*	*	*	-	*	*	*	7
Farrar, 2011	-	*	*	*	**	*	*	*	8

Very low risk of bias, points 9-10; Low risk of bias, points 7-8 ; Moderate risk of bias, points 5-6 ; High risk of bias, 0-4 points

Table 5 Assessment of article quality controlled randomized test (RCT) association of melanin and vitamin D

Article	Score Based on JBI Critical Appraisal for RCT													Overall Appraisal
First author, Year	1	2	3	4	5	6	7	8	9	10	11	12	13	
Au, 2014	Y	Y	Y	Y	Y	UC	Y	Y	Y	Y	Y	Y	Y	√
Rajakumar, 2016	Y	Y	Y	Y	Y	UC	Y	Y	Y	Y	Y	Y	Y	√
Ohlund, 2017	Y	Y	Y	Y	Y	UC	Y	Y	Y	Y	Y	Y	Y	√
Young, 2020	Y	Y	Y	Y	UC	UC	Y	Y	Y	Y	Y	Y	Y	√

Y: Yes; N: No; UC: Unclear; NA: Not applicable; √: Included; X: Excluded used the Fitzpatrick Skin Type questionnaire to measure melanin or skin pigment, which tends to be more subjective than other measurements of melanin index.

The researchers recommend conducting a systematic study using randomised controlled trials that control for additional or other factors to focus on the association between melanin and increased vitamin D concentration, thereby increasing validity and using articles with low research bias values. Furthermore, they suggest using a wider database to obtain more articles for further research. The public is advised to be aware of their skin pigment types, dark or light, in order to prevent vitamin D deficiency by taking vitamin D supplements if needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENT

None.

REFERENCES

1. Siddiqee MH, Bhattacharjee B, Siddiqi UR, MeshbahurRahman M. High prevalence of vitamin D deficiency among the South Asian adults: a systematic review and meta-analysis. BMC Public Health. 2021;21:1823.
2. Pulungan A, Soesanti F, Tridjaja B, Batubara J. Vitamin D insufficiency and its contributing factors in primary school-aged children in Indonesia, a sun-rich county. Annals of Pediatric Endocrinology and Metabolism. 2021;26(2):92–8.
3. Rimahardika R, Subagio HW, Wijayanti HS. Asupan vitamin D dan paparan sinar matahari pada orang yang bekerja di dalam ruangan dan di luar ruangan. Journal of Nutrition College. 2017;6:333.
4. Saptarini D. Status vitamin D pada remaja sehat usia 15-18 tahun di Kota Depok. Journal of Indonesian Medical Association Majalah Kedokteran Indonesia. 2019;69(2).
5. Aji AS, Erwinda E, Yusrawati Y, Malik SG, Lipoeto NI. Vitamin D deficiency status and its related risk factors during early pregnancy: a cross-sectional study of pregnant Minangkabau women, Indonesia. BMC Pregnancy Childbirth. 2019;19.
6. Oktaria V, Graham SM, Triasih R, Soenarto Y, Bines JE, Ponsonby AL, Danchin M. Thre prevalence and determinants of vitamin D deficiency in Indonesian infants at birth and six months of age. PLoS ONE. 2020; 15(10).
7. WHO. Vitamin D nutrition with a focus on the prevention of rickets and vitamin D deficiency in pregnant women [Internet]. World Health Organization; [cited 2020 May 23]. Available from: http://www.who.int/nutrition/events/2015_vit_d_workshop_pregnantwomen_21to24Apr15/en/
8. NIH. Office of Dietary Supplements - Vitamin D [Internet]. National Institutes of Health; [cited 2020 May 22]. Available from: https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/
9. Książek A, Zagrodna A, Słowińska-Lisowska M. Vitamin D, skeletal muscle function and athletic performance in athletes—A narrative review. Nutrients. 2019;11(8):1800.
10. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Berisha AT, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. European Journal of Clinical Nutrition. 2020; 74: 1498-1513.
11. Sizar O, Khare S, Goyal A, Bansal P, Givler A. Vitamin D Deficiency. Treasure Island (FL): StatPearls Publishing; 2020.
12. Sakamoto RR. Sunlight in vitamin D deficiency: Clinical implications. The Journal for Nurse Practitioners. 2019;15:282–5.
13. Bonilla C, Ness AR, Wills AK, Lawlor DA, Lewis SJ, Smith GD. Skin pigmentation, sun exposure and vitamin D levels in children of the Avon Longitudinal Study of Parents and Children. BMC Public Health. 2014;14:597.
14. Hameed A, Akhtar N. The skin melanin: An inhibitor of vitamin-D3 biosynthesis: With special emphasis with structure of skin. A mini review. Dermatology Case Reports. 2019;4:1.
15. Young AR, Morgan KA, Ho T-W, Ojimba N, Harrison GI, Lawrence KP, et al. Melanin has a small inhibitory effect on cutaneous vitamin D synthesis: A comparison of extreme phenotypes. Journal of Investigative Dermatology. 2020;140(1):1418-26.
16. Tawfik GM, Dila KAS, Mohamed MYF, Tam DNH, Kien ND, Ahmed AM, et al. A step by step guide for conducting a systematic review and meta-analysis with simulation data. Tropical Medicine and Health. 2019;47:46.
17. Umar M, Sastry KS, Ali FA, Al-Khulaifi M,

Wang E, Chouchane AI. Vitamin D and the pathophysiology of inflammatory skin diseases. Skin Pharmacology and Physiology. 2018;31:74–86.
18. Gopal-Kothandapani JS, Evans LF, Walsh JS, Gossiel F, Rigby AS, Eastell R, et al. Effect of vitamin D supplementation on free and total vitamin D: A comparison of Asians and Caucasians. Clinical Endocrinology (Oxf). 2019;90:222–31.
19. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. World Journal of Meta-Analysis. 2017;5(4):80–4.
20. Martin J. © Joanna Briggs Institute 2017 Critical Appraisal Checklist for Cross Sectional Studies, Cohort Studies, and Randomized Controlled Trials. 2017;7.
21. Hall LM, Kimlin MG, Aronov PA, Hammock BD, Slusser JR, Woodhouse LR, et al. Vitamin D intake needed to maintain target serum 25-hydroxyvitamin D concentrations in participants with low sun exposure and dark skin pigmentation is substantially higher than current recommendations. The Journal of Nutrition. 2010;140(3):542–50.
22. Chan J, Jaceldo-siegl K, Fraser GE. Determinants of serum 25 hydroxyvitamin D levels in a nationwide cohort of blacks and non-Hispanic whites. Cancer Causes & Control. 2010;21(4):501–11.
23. Farrar MD, Kift R, Felton SJ, Berry JL, Durkin MT, Allan D, et al. Recommended summer sunlight exposure amounts fail to produce sufficient vitamin D status in UK adults of South Asian origin. The American Journal of Clinical Nutrition. 2011;94(5):1219–24.
24. Murphy AB, Kelley B, Nyame YA, Martin IK, Smith DJ, Castaneda L, et al. Predictors of serum vitamin D levels in African American and European American men in Chicago. Am J Mens Health. 2012;6(5):420–6.
25. Au LE, Harris SS, Dwyer JT, Jacques PF, Sacheck JM. Association of serum 25-hydroxyvitamin D with race/ethnicity and constitutive skin color in urban schoolchildren. Journal of Pediatric Endocrinology & Metabolism. 2014;27(11-12):1095–100.
26. Green TJ, Li W, Barr SI, Jahani M, Chapman GE. Vitamin D supplementation is associated with higher serum 25OHD in Asian and White infants living in Vancouver, Canada. Maternal & Child Nutrition. 2015;11(2):253–9.
27. Rajakumar K, Moore CG, Yabes J, Olabopo F, Haralam MA, Comer D, et al. Estimations of dietary vitamin D requirements in black and white children. Pediatric Research. 2016;80(1):14–20.
28. Öhlund I, Lind T, Hernell O, Silfverdal S-A, Karlsland Åkeson P. Increased vitamin D intake differentiated according to skin color is needed to meet requirements in young Swedish children during winter: a double-blind randomised clinical trial. The American Journal of Clinical Nutrition. 2017;106(1):105–12.
29. Cabral MA, Borges CN, Coelho Maia JM, Aires CAM, Bandeira F. Prevalence of vitamin D deficiency during the summer and its relationship with sun exposure and skin phototype in elderly men living in the tropics. Clinical Interventions in Aging. 2013;8:1347–51.
30. Dix CF, Bauer JD, Martin I, Rochester S, Romero BD, Prins JB, et al. Association of Sun Exposure, Skin Colour and Body Mass Index with Vitamin D Status in Individuals Who Are Morbidly Obese. Nutrients. 2017;9(10):1094.
31. Sarkar S, Gaddameedhi S. Solar UV-induced DNA damage response: Melanocytes story in transformation to environmental melanomagenesis. Environmental and Molecular Mutagenesis. 2020;61(7): 736-51.
32. Webb AR, Kazantzidis A, Kift RC, Farrar MD, Wilkinson J, Rhodes LE. Colour CountsL Sunlight and Skin Types as Drivers of Vitamin D Deficiency at UK Latitudes. Nutrients. 2018;10(4): 457.