Vitamin D deficiency in South-East Asian children: a systematic review

Vicka Oktaria ,[1,2] Dwi Astuti Dharma Putri ,[2] Zulfikar Ihyauddin ,[2] Madarina Julia ,[3] Dian Caturini Sulistyoningrum ,[4] Poh Bee Koon ,[5] Margaret Danchin ,[6,7,8] Indah Kartika Murni [2,3]

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For numbered affiliations see end of article.

Correspondence to
Dr Vicka Oktaria, Department of Biostatistics, Epidemiology and Population Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Sleman, Daerah Istimewa Yogyakarta, Indonesia; vicka.oktaria@ugm.ac.id

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ABSTRACT

Objective To describe the prevalence and determinants of vitamin D deficiency (VDD) among healthy children aged between 0 and 18 years living in South-East Asia (SEA).

Design We systematically searched Ovid MEDLINE and Ovid EMBASE for observational studies assessing VDD among healthy children in the SEA region as the primary or secondary outcome from database inception to 6 April 2021. PubMed was used for e-pubs and publications not indexed in Medline. Publications that included abstracts in English were included. We performed a systematic review to describe the prevalence of VDD in SEA children.

Results Our initial search identified 550 publications with an additional 2 publications from manual screening. Of those, 21 studies from 5 different countries (Thailand, Indonesia, Vietnam, Malaysia and Cambodia) were summarised and included in forest plots. The prevalence of VDD (<50 nmol/L) ranged from 0.9% to 96.4%, with >50% of newborns having VDD, and severe VDD (<30 nmol/L) ranged from 0% to 55.8%. Female sex and urban living were the most common determinants of VDD.

Conclusions VDD among healthy children living in the SEA region is common. Efforts to detect VDD and the implementation of preventive measures, including education on safe sun exposure and oral vitamin D supplementation or food fortification, should be considered for key target groups, including adolescent females and pregnant and lactating women to improve the vitamin D status of newborns.

Protocol registration number This study is registered with PROSPERO (CRD42020181600).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Vitamin D deficiency (VDD) is a global public health issue.
⇒ VDD has been recently linked with increased risks for various skeletal and non-skeletal diseases.
⇒ Multicountry data on prevalence of VDD among South-East Asian (SEA) children are lacking.

WHAT THIS STUDY ADDS

⇒ VDD in healthy SEA children varies among countries and age groups but is most common in newborns (52%–90%).
⇒ Detection and preventive measures of VDD, particularly among newborns and adolescent females, should be implemented to reduce the risks arising from VDD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Global consensus on an agreed threshold level for VDD and standardisation of assays to measure vitamin D are urgently needed.
⇒ In subpopulations in SEA where prevalence of VDD (<30 nmol/L) exceeds 20%, public health interventions are crucial to reduce the burden of VDD.
⇒ Interventions, such as safe sunlight exposure, food fortification and supplementation, are encouraged, particularly for high-risk groups, and should be developed through multisectoral programmes.

INTRODUCTION

Vitamin D deficiency (VDD) is a global public health issue.[1] During periods of rapid growth, such as infancy and prepuberty, severe VDD can lead to demineralisation of the skeleton and deformities, a condition known as rickets.[2] In young children, rickets may present as bow legs, delayed eruption of teeth and hypocalcaemic seizures,[3] while in adolescence, it presents as diffuse bone and muscle pain, deformities of lower extremities and generalised muscle weakness despite normal radiological findings.[4] Rickets has recently re-emerged in children possessing darker skin tones, who have low exposure to direct sunlight and poor vitamin D intake.[5 6]

More recently, the non-osseous complications of VDD have also been highlighted including increases in acute respiratory infections, cardiovascular diseases and all-cause mortality.[7–12] Children with VDD have been reported to be at risk of developing severe pneumonia,[13] or failing to respond to standard pneumonia therapy,[14] due to weakened immunity and softened ribs which limit effective breathing and clearance of pathogens.[3]

Vitamin D studies in the South-East Asia (SEA) region have highlighted the importance of VDD in the region, but synthetic estimates of regional VDD burden in children are not yet available.[15 16] Despite abundant sunlight, there are lifestyle and cultural beliefs that contribute to VDD in the region.[15] Strategies to maintain adequate vitamin D levels in

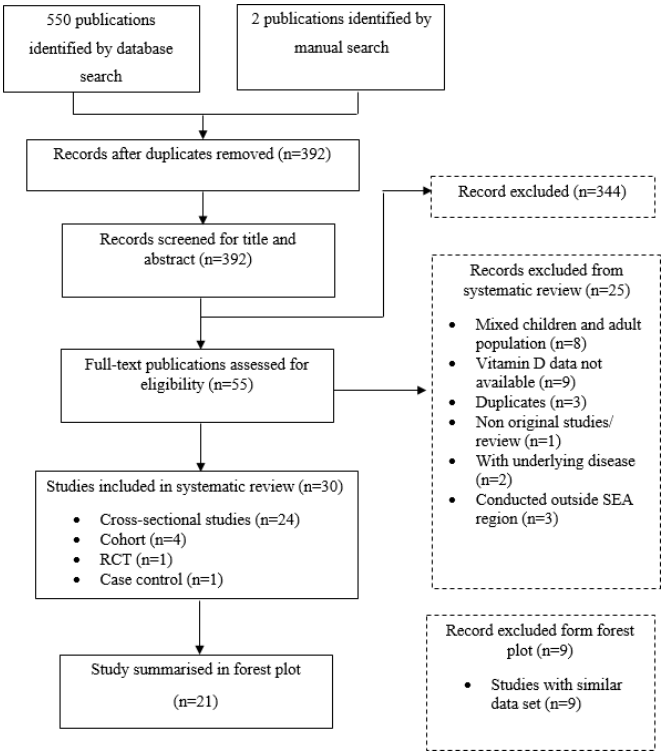

Figure 1 Flow chart of selection of eligible publications. RCT, randomised controlled trial; SEA, South-East Asia.

the region should comprise public health interventions that are affordable and achievable and sustainable.[17] With clear public health and clinical benefits of optimal vitamin D status, there is an urgent need to identify target age groups at risk of VDD in children and the associated determinants to enable effective planning for preventive or interventional measures.

We systematically reviewed the existing publications which included children in the SEA region to describe the prevalence and major determinants of VDD in the region.

METHODS

Search strategy and eligibility criteria

We systematically searched Ovid MEDLINE and Ovid EMBASE, from database inception to 6 April 2021, using thesaurus and keywords; and PubMed using keywords-only to retrieve e-pubs and items not-indexed in Medline, for studies assessing the prevalence of VDD in children from the SEA region (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, The Philippines, Singapore, Thailand, Timor-Leste and Vietnam). Eligibility criteria included original studies with an abstract available in English, including case-control studies, cross-sectional surveys and cohort studies that reported the prevalence/incidence of VDD among healthy children aged 0–18 years residing in the SEA region. For randomised controlled trials (RCTs) and case-control studies, only vitamin D status of the control/non-intervention groups were included. We excluded case reports/series, letters or reviews. A healthy child was defined as any child without any known significant health problems, or conditions, or medications that would otherwise affect the metabolism of vitamin D.

Keywords and appropriately related Medical Subject Headings terms were used and modified to suit each database (online supplemental file 1). A manual search of each database was conducted to complement the systematic search with similar keywords.

Selecting studies and collecting data

Titles and abstracts were screened independently by two investigators (VO and DADP) using Covidence (https://www.covidence.org/) and all publications that met the eligibility criteria were retrieved in full-text format. Data extraction, that is, author's name, study design, location, age, vitamin D quantification methods and determinants of VDD were recorded by two investigators (VO and DADP). Any discrepancies were resolved through discussions with a third investigator (ZI). If the required information was not available in the published articles, data were personally requested from the authors.

Risk of bias assessment

Risk of bias was assessed using the bias tool by Hoy *et al*[18] and modified according to the recent published meta-analysis study in African children.[19] Each study was assessed, and categorised into low, moderate or high risk.

Outcome measures

VDD was defined as serum (or plasma) 25-hydroxyvitamin D (25(OH)D) concentrations <50 nmol/L (equivalent to <20 ng/dL) with the main consideration being a vitamin D level adequate enough to maintain optimal bone health without contributing to other health outcomes.[20] In the subgroup analysis, we reported the prevalence of VDD below <30 nmol/L if >20% of the target population had a level below 30 nmol/L[21], as this was the chosen cut-off for public health intervention. These data were only included when original data from authors were obtainable. Studies that reported serum vitamin D levels with ng/dL were converted to nmol/L, with every 1 ng/dL having an equivalent value of ~2.5 nmol/L.

When needed, recalculations for prevalence of VDD or mean serum vitamin D levels were performed, for example:

- Studies using different cut-off criteria to define VDD, such as 25(OH)D level <30 nmol/L as deficient and 30–49.9 nmol/L as insufficient. In such cases, percentages from both groups were combined to fulfil the current study criteria for VDD <50 nmol/L.
- Prevalence (or mean) that was reported in a subgroup (ie, rural/urban) was calculated by the following formula:

$$\bar{p} = \frac{(p_1 \times n_1) + \ldots + (p_i \times n_i)}{N} \text{ or } \bar{x} = \frac{\left(\bar{x}_1 \times n_1\right) + \ldots + \left(\bar{x}_i \times n_i\right)}{N}$$

$\bar{p}$=VDD prevalence reported in the study.
$\bar{x}$=mean of 25(OH)D level from all participants in the study.
n=the number of participants in the subgroup.
N=total participants tested for vitamin D level.

Data analysis

The data analysis was performed using a STATA, V.16 (StataCorp, Texas, USA). When multiple publications used a similar study dataset (overlapping of samples) with a single vitamin D measurement performed in participants, only the publication with the most complete dataset was included. We initially attempted to perform a meta-analysis with the random-effects models; plotting the pooled prevalence of VDD in forest plots, and showing the estimated size effect of prevalence or baseline prevalence (for prospective studies) of VDD with a 95% CI. However, due to high between-study heterogeneity, with I^2 values >75%, prevalence or incidence ranges were presented instead. Substantial between-study heterogeneities were also present during meta-analysis for VDD prevalence by age group, gender, countries and residency. Publication bias were assessed based on visual or analytical detection of asymmetry in a funnel plot. We used the Egger's test for bias with $p<0.05$ considered as significant publication bias.

Table 1 Vitamin D deficiency (VDD) among children in SEA region (n=30)

Study	Year of study	Design	N§	Location	Age (years)	Quantification methods	Prevalence/ Cumulative incidence VDD‡ (50 nmol/L) (%)	Prevalence/Cumulative incidence VDD§ (30 nmol/L) (%)	Mean of serum 25(OH)D (nmol/L)	Risk factors associated with VDD
Febriani A *et al*[69]	2019	Case-control	40	Indonesia	0.5–5	ELISA	n/a	n/a	49.77 (control)	n/a
Irwinda and Andardi¶[57]	2017–2019	Cross-sectional	30	Indonesia	Newborn	LC-MS/MS	52.4	n/a	44	n/a
Chuc *et al*¶[22]	2017	Cross-sectional	327	Vietnam	1–3	ELISA	47.7	0	81.3	Older age
Ariyawatkul and Lersbuasin¶[46]	2016–2017	Cross-sectional	94	Thailand	Newborn	Chemiluminescent microparticle immunoassay	89.3	20.2	37.1	Low maternal vitamin D level
Oktaria *et al* ¶††[35]	2015–2017	Cohort	344 (at birth) 255 (6 months)	Indonesia	Newborn and 6 months	LC-MS/MS	90 (at birth) 13 (6 months)	55.8 (at birth) 4.3 (6 months)	30 (at birth) 77 (6 months)	Lower cumulative skin-sun exposure score, severe VDD at birth and exclusive breast feeding
Loeb *et al*¶[36]	2013–2016	RCT (baseline)	1095	Vietnam	3–17	Diasorin	16.8	n/a	65.5	n/a
Yani *et al*¶[24]	2014–2015	Cross-sectional	100	Indonesia	<5	ELISA	21	1.78	67.5	n/a
Quah *et al**¶[25]	2014	Cohort	1016	Malaysia	15	Automated direct competitive chemiluminescent immunoassay	33	2.6	59.4	Female sex, Malay and Indian ethnicity, and wearing long sleeves
Smith *et al*¶[51]	2014	Cross-sectional	781	Cambodia	0.5–5	ELISA	13.4	n/a	91.1	Urban living and older age
Diana *et al*¶[26]	2013–2014	Cohort	116	Indonesia	6 and 12 months	Isotope-dilution LC tandem MS	0.9 (6 months) 4.3 (12 months)	0 (6 months and 12 months)	89.7† (6 months) 83.2† (12 months)	n/a
Al-Sadat *et al**¶[44]	2012	Cross-sectional	1361	Malaysia	12–13	ECLIA	92.6	n/a	29.2	Female sex, Indian ethnicity, urban living and obesity (wider waist circumference)
Rahmadhani *et al*¶[45]	2012	Cross-sectional	678	Malaysia	13	ECLIA	70	n/a	42.3	Female sex, high BMI
Pulungan *et al*¶[54]	2012	Cross-sectional	120	Indonesia	7–12	Diasorin	39.2	1.6	54.6	Less time spent outdoors
Nguyen *et al*[50]	2012–2016	Cross-sectional	794	Vietnam	6–14	HPLC/MS	30.6	n/a	67.39	Female sex, overweight/ obese
Poh *et al*¶‡[37]	2010–2011	Cross-sectional	2016	Indonesia, Malaysia, Thailand, Vietnam	>2	Diasorin (Malaysia, Thailand), HPLC (Vietnam), immunoactivity detection system (Indonesia)	42.14	n/a	56.1	Female sex, older age, urban living, religion, higher BMI and region
Senaprom *et al*‡[39]	2011	Cross-sectional	477	Thailand	3–13	Diasorin	31.9	n/a	60.1	Female sex, Muslim religion, obesity, sun exposure <30 min/day in weekdays (end)
Ernawati and Budiman *et al*‡[40]	2011	Cross-sectional	349	Indonesia	2–13	EIA	45.1	n/a	52.6	Female sex, older age, less time spent outdoors
Reesukumal *et al*¶‡[28]	2011–2012	Cross-sectional	159	Thailand	6–12	ECLIA	19.5	0.6	64	Higher BMI, higher body fat percentage, higher parathyroid hormone
Sandjaja *et al*‡[33]	2011	Cross-sectional	276	Indonesia	2–12	Not specified	43.6	n/a	52.5	Female sex
Rojroongwasinkul *et al*‡[38]	2011	Cross-sectional	628	Thailand	3–13	Diasorin	33.5	n/a	n/a	Urban living
Le Nguyen *et al*‡[29]	2011	Cross-sectional	574	Vietnam	6–12	HPLC	50.4	n/a	n/a	n/a
Nguyen Bao *et al*‡[30]	2010–2011	Cross-sectional	384	Indonesia, Malaysia, Thailand, Vietnam	1–12	Diasorin (Malaysia, Thailand), HPLC (Vietnam), immunoactivity detection system (Indonesia)	45.8	17.5	55.7	Higher dairy daily consumption
Poh *et al*‡[27]	2010–2011	Cross-sectional	2936	Malaysia	4–12	Diasorin	47.5	n/a	54.7	Female sex, urban living, older age
Laillou *et al*¶[43]	2010	Cross-sectional	485	Vietnam	<5	HPLC	57.3	20.6	43.4	n/a
Poomthavorn *et al*¶[31]	2008–2009	Cross-sectional	179	Thailand	<18	HPLC	11 (obese) 10 (non-obese)	0 (obese and non-obese)	70.4 (obese) 68.9 (non-obese)	Older age, lower weight circumference

Continued

Table 1 Continued

Study	Year of study	Design	N§	Location	Age (years)	Quantification methods	Prevalence/ Cumulative incidence VDD‡ (50 nmol/L) (%)	Prevalence/Cumulative incidence VDD§ (30 nmol/L) (%)	Mean of serum 25(OH)D (nmol/L)	Risk factors associated with VDD
Khor *et al*¶[42]	2008	Cross-sectional	402	Malaysia	7–12	Diasorin	72.4	n/a	n/a	Higher BMI in boys, female sex
Houghton *et al*¶[49]	2002–2003	Cross-sectional	529	Thailand	6–14	LC-MS/MS	4	n/a	72.7†	Older female
Tangngam *et al*¶[47]	n/a	Cross-sectional	28	Thailand	4.8–17.2	Chemiluminescence assay	96.4	n/a	66.5**	n/a
Soesanti *et al*¶[34]	n/a	Cross-sectional	120	Indonesia	7–12	Not specified	39.2	n/a	n/a	Female sex
Hussain and Elnajeh¶[32]	n/a	Cross-sectional	361	Malaysia	13–18	CLIA	60.1	16.3	49	Female sex, Malay ethnicity

VDD was defined when serum 25(OH)D <50 nmol/L[20]
*Data from MyHeARTs, both studies were included because eventhough data were derived from the same study, the time point was different.
†Geometric mean.
‡Data from SEANUTS. Poh *et al*[37] was chosen as SEANUTS representative, as it provides most of the countries prevalence and meet our criteria to define VDD.
§Total participants that had vitamin D testing.
¶Included in the forest plot.
**Median.
††Data from IPADS, both papers present the same result, Oktaria *et al*[35] was chosen as it is the first one published.
BMI, body mass index; ECLIA, electrochemiluminescence immunoassay; EIA, enzyme immunoassay; HPLC, high performance liquid chromatograph; IPADS, The Indonesian Pneumonia and vitamin D Study; LC-MS/MS, liquid chromatography-mass spectrometry; MyHeARTs, Malaysian Health and Adolescents Longitudinal Research Study; n/a, not available; 25(OH)D, 25-hydroxyvitamin D; RCT, randomised controlled trial; SEA, South-East Asia; SEANUTS, South-East Asian Nutrition Survey.

Table 2 Vitamin D deficiency (VDD) prevalence among children in SEA region based on age group division (n=30)

Study	VDD (<50 nmol/L) prevalence or cumulative incidence based on age group
Febriani A *et al*[69]	6 months–5 years: n/a
Irwinda and Andardi[57]	Newborn: 52.4%
Chuc *et al*[22]	12 to <24 months: 42.5%, 24–36 months: 53.1%
Ariyawatkul and Lersbuasin[46]	Newborns: 89.3%
Oktaria *et al*[23]	Newborns: 90%, 6 months: 13%
Loeb *et al*[36]	3–17 years: 16.8%
Yani F *et al*[24]	<5 years: 21%
Quah *et al*[25]	15 years: 33%
Smith *et al*[51]	6–11 months: 7.3%, 12–23 months: 11.3%, 24–59 months: 12.9%, 60+ months: 19.6%
Diana *et al*[26]	6 months: 0.9%, 12 months: 4.3%
Al-Sadat *et al*[44]	12–13 years: 92.6%
Rahmadhani *et al*[45]	13 years: 70%
Pulungan *et al*[54]	7–12 years: 39.2%
Nguyen *et al*[50]	6–14 years: 67.39%
Poh *et al**[37]	>2 years: 48%
Senaprom *et al**[39]	3–13 years: 31.9%
Ernawati and Budiman*[40]	2.0–2.9 years: 49.2%, 3.0–5.9 years: 37.2%, 6.0–8.9 years: 45.8%, 9.0–12.9 years: 50.7%
Reesukumal *et al**[28]	6–12 years: 19.5%
Sandjaja *et al**[33]	2.0–4.9 years: 38.8%, 5.0–12 years: 45.8%
Rojroongwasinkul *et al**[38]	3.0–5.9 years: urban 31.3%, rural 24.5%, 6.0–12.9 years: urban 52.2%, rural 29.2%
Le Nguyen *et al**[29]	6–12 years: 48%–53%
Nguyen Bao *et al**[30]	1–12 years: 46.6%
Poh *et al**[27]	4.0–6.9 years: urban 34.6%, rural 17.9%, 7.0–12 years: urban 57.3%, rural 45.6%
Laillou *et al*[43]	<5 years: 57.3%
Poomthavorn *et al*[31]	<18 years: 11.2%
Khor *et al*[42]	7–12 years: 72.4%
Houghton *et al*[49]	6–14 years: 4%
Tangngam *et al*[47]	4.8–17.2 years: 96.4%
Soesanti *et al**[34]	Not specified
Hussain and Elnajeh[32]	13–18 years: 16.1%

*Data from SEANUTS. Poh *et al*[37] was chosen as SEANUTS representative, as it provides most of the countries prevalence and meet our criteria to define VDD.
†Data from MyHeARTs, both studies were included because eventhough data were derived from the same study, the time point was different.
‡Data from IPADS, both papers present the same result, Oktaria *et al*[35] was chosen as it is the first one published.
IPADS, The Indonesian Pneumonia and vitamin D study; MyHeARTs, Malaysian Health and Adolescents Longitudinal Research Study; n/a, not available; 25(OH)D, 25-hydroxyvitamin D; SEA, South-East Asia; SEANUTS, South-East Asian Nutrition Survey.

This study is registered with PROSPERO (CRD42020181600) with the protocol available online.

RESULTS

Our initial systematic search identified 550 publications, with two additional publications identified through manual search. Of those, 30 were included in the final systematic review. We further contacted the authors from 27 publications that did not provide detailed information as needed, including details regarding the proportion of participants with vitamin D levels <30 nmol/L. A total of 11 authors responded,[22–32] with 5 providing information on proportion of participants with vitamin D <30 nmol/L.[23–25 28 30] Twenty-one included studies were further summarised and plotted into forest plots for study exclusion as provided in figure 1. The inter-rater agreement of study selection was 85% with four studies requiring assessment from a third investigator. Two of 30 studies were identified as having a moderate risk of bias[33 34] while 28 (92%) had a low risk of bias (online supplemental file 2).

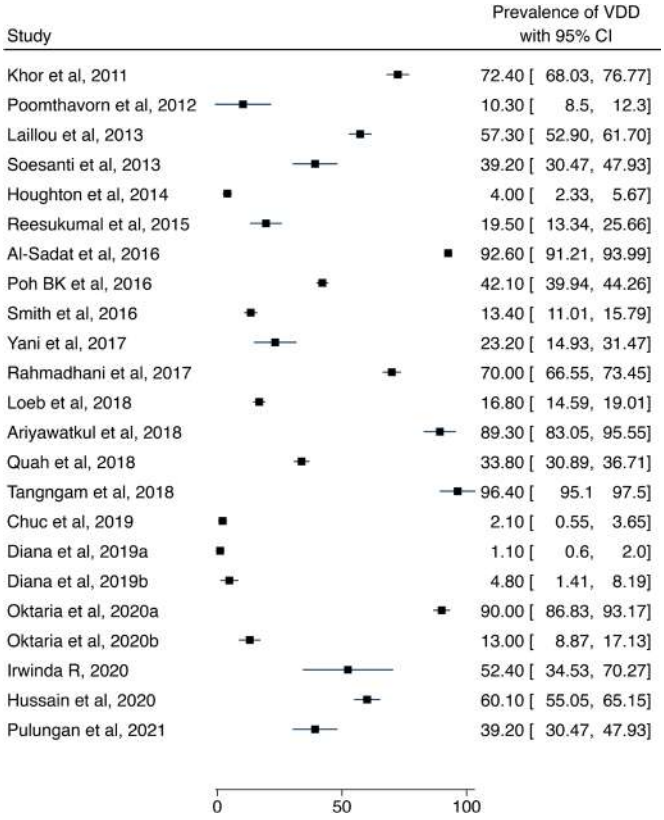

Figure 2 Forest plot: vitamin D deficiency (VDD) in South-East Asia region (n=21 studies) using a cut-off <50 nmol/L. Cohort studies with multiple vitamin D measurements were presented for each measurement (studies by Diana *et al* and Oktaria *et al*).

Study characteristics

The majority of studies (24/30; 80%) were cross-sectional in design except for four cohort studies,[23 25 26 35] and one[36] reported baseline data from an RCT, with a wide range of vitamin D assays used (table 1). Eight of 30 studies included were part of the South-East Asian Nutrition Survey (SEANUTS),[27 29 30 33 37–40] a comprehensive survey, studying growth, nutrition and food intake, conducted in Indonesia, Malaysia, Thailand and Vietnam.[41] The age range among studies was diverse, from newborns to 18 years of age (table 2).

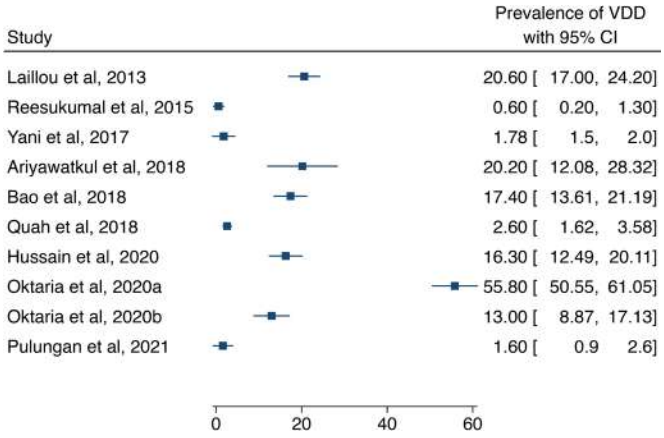

Figure 3 Forest plot: vitamin D deficiency (VDD) in South-East Asia region (n=9 studies) using a cut-off <30 nmol/L. Cohort studies with multiple vitamin D measurements were presented for each measurement (studies by Oktaria *et al*).

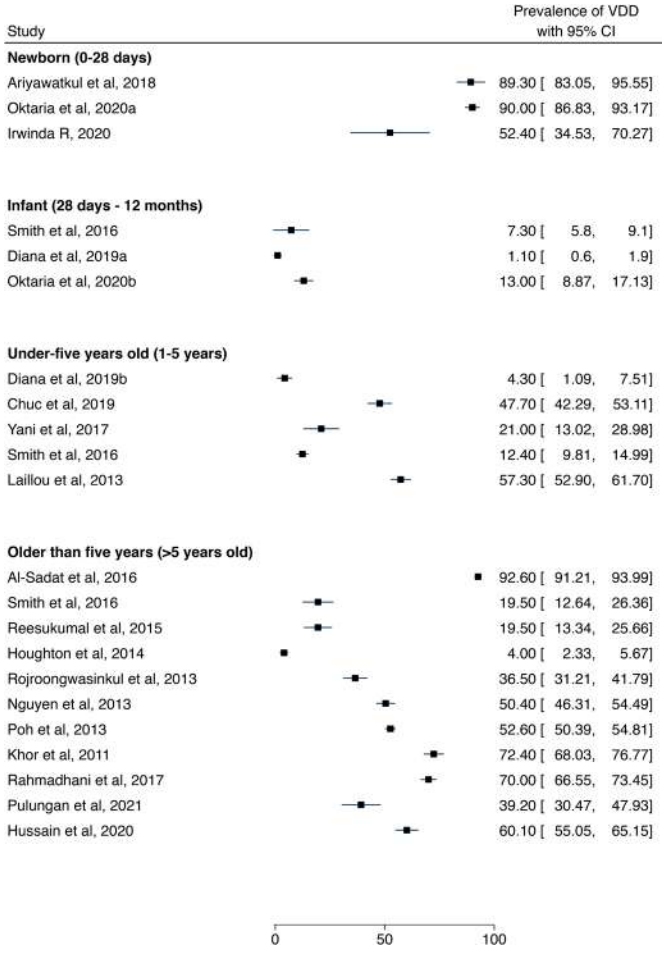

Figure 4 Subgroup analysis: vitamin D deficiency (VDD) in South-East Asia region by age group (n=20 studies). Cohort studies with multiple vitamin D measurements were presented for each measurement (studies by Diana *et al* and Oktaria *et al*), the prevalence of VDD in the study by Smith *et al* was reported by age group. The test of group differences for VDD by age group was Q_(3)=49.57, p<0.001.

Fourteen studies required prevalence recalculation, with nine studies reporting vitamin D in subgroups (ie, by gender, urban/rural or by country)[24 27 29–31 33 36–38] and five studies employed different cut-offs for VDD (<37.5 nmol/L, table 1).[39 42–45] Ten of 20 studies required mean re-calculation; with three studies reporting vitamin D levels in ng/dL units[22 46 47] and seven studies reporting vitamin D level in subgroups.[27 29 31 33 36 37 44] For each forest plot, only one SEANUTS study was included, as relevant.

The prevalence of VDD in SEA children

The prevalence of VDD ranged from 0.9% to 96.4% based on a cut-off of <50 nmol/L (figure 2), and from 0% to 55.8% based on a cut-off of <30 nmol/L (figure 3). Pooled results were not presented due to significant between-study heterogeneity (I^2=99.9%, p<0.001).

The prevalence of VDD varied widely within age groups (figure 4), but was consistently high in newborns, with at least one in every two newborns having VDD. Due to limited data from the original studies, we were unable to separate adolescents (aged between 10 and 19 years) from children ≥5 years.[48] However, four studies exclusively reported the prevalence of VDD in adolescents (online supplemental file 3).[25 32 44 45] The prevalence of VDD by country (online supplemental file 4), sex (figure 5) or residence (online supplemental

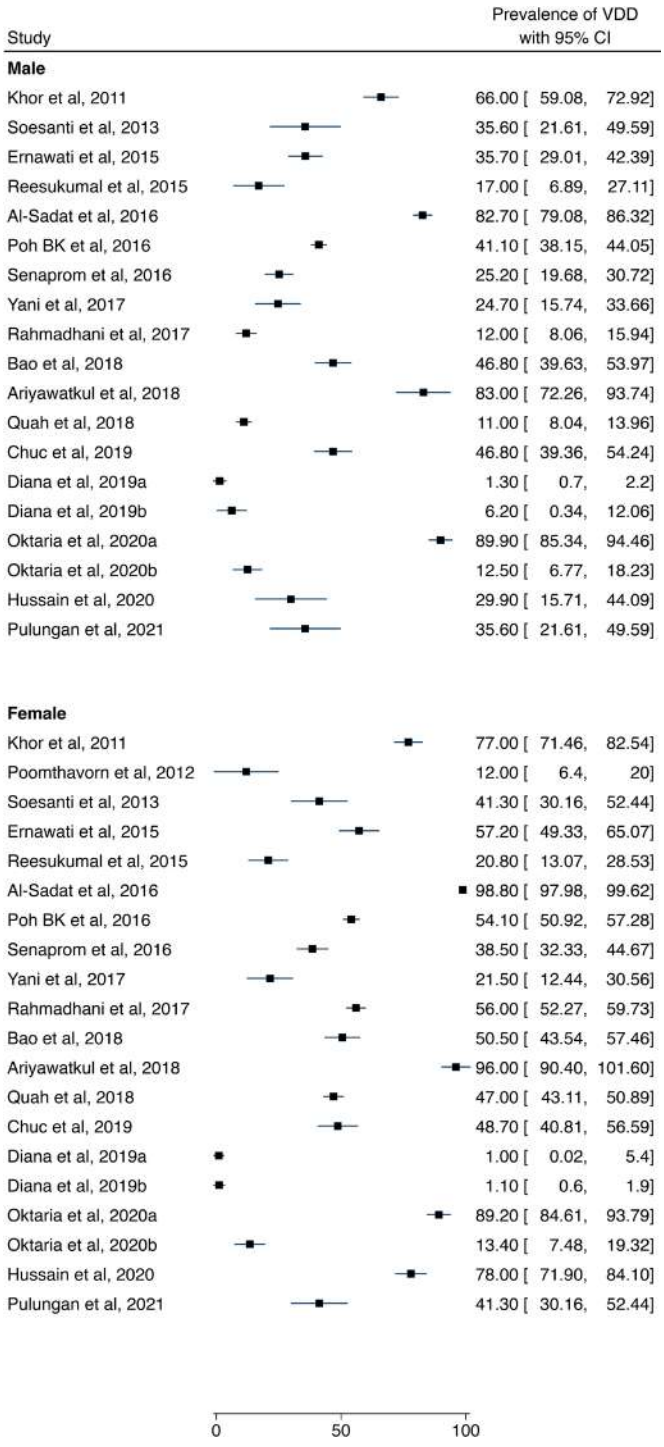

Figure 5 Subgroup analysis: vitamin D deficiency (VDD) in South-East Asia region by sex (n=18). Cohort studies with multiple vitamin D measurements were presented for each measurement (Oktaria *et al*). The test of group differences for VDD by sex was Q_b=1.27, p=0.26.

file 5) was hard to interpret due to a large variation among reported prevalence estimates. Four publications from three cohort studies reported multiple measurements of serum vitamin D in their participants at different time.[25 26 35 44]

The determinants of VDD

The most common reported risk factors for VDD in the region were female sex,[25 27 33 34 37 39 40 42 44 45 49 50] older children,[22 27 31 37 40 49 51] urban living,[27 37 38 44 51 52] covered-up clothing for religious purposes,[37 39 53] exposure to sunlight <30 min/day[35 39 40 54] and obesity[31 37 42 44 45] (table 1). Subgroup analysis by gender and residence are presented in figure 5 and online supplemental file 5, respectively.

Publication bias of vitamin D deficiency

The funnel plot was asymmetric (online supplemental file 6) due to high between-study heterogeneity and various reported effect sizes. Egger's test showed a p value of 0.96 indicating no statistical evidence of publication bias.

DISCUSSION

VDD is very common in SEA children, with female sex and those living in urban areas the most common reported risk factors, consistent with recent findings from an African meta-analysis.[19] Pooled effects were not reported in the current study due to substantial heterogeneity between studies.

The prevalence of VDD in SEA children varies among age groups. Of four studies that exclusively report vitamin D status for the adolescent age group,[25 32 44 45] three reported a high prevalence of VDD (>60% were <50 nmol/L). While teenagers may enjoy outdoor sports, in many countries female teenagers begin to dress more conservatively, covering-up for religious purposes.[3] Female adolescents have been consistently reported to be at risk of developing VDD in most countries,[25 33 39 40 42] with a 4% decline of serum vitamin D level for each year of increasing age.[49] Furthermore, there are cultural practices that are strongly affected by religion, and also society's perception of fair skin as a standard for female beauty in the SEA region.[51] The practice of sunlight avoidance (ie, staying in the shade or under an umbrella, wearing sun protection) or the use of covered-up garments such as veils for religious purposes, is evident among SEA females.[25 33 39 40 42 55] In addition to sun-avoidance, air pollution in urban regions has been reported to be associated with VDD in children due to attenuation of UVB light reaching the earth's surface which reduces cutaneous photosynthesis of vitamin D.[56]

Particular attention is needed to support adequate transplacental transfer of vitamin D during the antenatal period[26] as interventions during pregnancy are an important determinant of neonatal vitamin D status. Mothers are the only source of fetal vitamin D during intrauterine life with maternal and cord blood vitamin D levels highly correlated.[46] Nine out of 10 newborns in Indonesia and Thailand were reported to have VDD[35 46 57] and as expected, VDD is also common in pregnant women in Thailand and Indonesia.[58 59] There is a concern that prenatal transfer of vitamin D might be impeded by maternal sunlight-exposure behaviour.[35] It has been reported that a maternal vitamin D status ≥50 nmol/L among white skinned women living in northern latitudes protects newborn infants from very low vitamin D status at birth.[60]

Given that the skin cancer rate in SEA is lower than Western population,[60] cutaneous vitamin D photoconversion should be optimised as the primary source of vitamin D.[61 62] A combination of larger total body surface area exposed to the sun and higher UVB intensity was correlated to higher vitamin D levels in pregnant women and infants in Indonesia.[35 63] Pregnant women are recommended to get sunlight exposure for half an hour/day between 10:00 and 13:00 hours to improve the vitamin D status in their newborns (approximately 1 hour for females with covered-up garments).[63] Infant's skin, however, is more sensitive in nature and it is generally advised that infants, especially those with light skin, should not be exposed to direct sunlight.[64]

In many high-income countries, vitamin D supplementation for infants, pregnant or nursing mothers are preferred over vitamin D generated by direct sunlight exposure.[20 65]

Dietary intake of foods that are naturally rich in vitamin D, or food fortification with vitamin D should be encouraged. Many children in the SEA consume <1% of the recommended daily vitamin D intake.[27 43] The availability of natural vitamin D-rich food sources in the region is limited with low and infrequent consumption of meat and dairy products.[39 66] Foods with the minimum recommended vitamin D intake of 400 IU vitamin D per 100 g consumption include fish, particularly milkfish, and eggs.[66] However, milkfish has as a high sodium content and should not be consumed too frequently.

With low availability of natural vitamin D-rich foods, food fortification and targeted supplementation should be considered. Detection of a prevalence of >20% of VDD <30 nmol/L in the overall population or within subgroups, or >1% of X-ray confirmed rickets in infants or children in the absence of vitamin D testing, have been suggested by experts as an indicator to start preventive public health actions.[21] Vitamin D can be added to dairy products, edible oils, flour or co-fortified with vitamin A,[21] but these efforts should be conducted through multisectoral programming with strong coordination between national government and private sectors.[67]

Although the VDD cut-off threshold of <30 nmol/L is used as a signal for public health action, limited published studies have used this threshold when they reporting VDD. There is also a lack of global consensus on the agreed thresholds level for VDD, insufficiency and adequacy due to complexity around precision and standardisation of various laboratory methods and assays to measure 25(OH)D.[68] Such consensus would aid future review and meta-analyses on the burden of VDD.

Although efforts have been made for a thorough search and identification of published studies in SEA regions, some countries (eg, Laos, Brunei Darussalam and Timor-Leste) were lacking relevant studies. The large heterogeneity between studies may be due to the wide variability of methods for vitamin D quantification or sociodemographic factors.

CONCLUSION

VDD is common in SEA children, with newborns and female adolescents most at risk. Improving vitamin D status might be delivered by 'safe' sunlight exposure practices, increasing vitamin D content in the diet or oral supplementation. The practice of vitamin D supplementation to improve vitamin D status of newborns should be started during pregnancy or postnatally during the period of breast feeding. With limited natural vitamin D-rich food sources in the SEA populations, food fortification or supplementation may need to be considered.

Author affiliations
[1]Department of Biostatistics, Epidemiology and Population Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Sleman, Daerah Istimewa Yogyakarta, Indonesia
[2]Center for Child Health-Pediatric Research Office, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Sleman, Daerah Istimewa Yogyakarta, Indonesia
[3]Child Health Department, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Sleman, Daerah Istimewa Yogyakarta, Indonesia
[4]Department of Nutrition and Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Sleman, Daerah Istimewa Yogyakarta, Indonesia
[5]Centre for Community Health Studies (ReaCH), Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur, Selangor, Malaysia
[6]Department of Paediatrics, The University of Melbourne, Melbourne, Victoria, Australia
[7]Murdoch Children's Research Institute, Melbourne, Victoria, Australia
[8]Department of General Medicine, Royal Children's Hospital, Melbourne, Victoria, Australia

Contributors Conceptualisation: VO, MJ, DCS, MHD, IM. Data curation: VO, DADDP, ZI. Formal analysis: VO, DADDP, ZI. Supervision: IM, MJ, MHD. Writing—original draft: VO. Writing—review and editing: VO, MD, IM, MJ, DCS, DADDP, ZI, BKP. Guarantor: VO.

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ORCID iDs
Vicka Oktaria http://orcid.org/0000-0002-3556-3028
Dwi Astuti Dharma Putri http://orcid.org/0000-0002-5225-8834
Zulfikar Ihyauddin http://orcid.org/0000-0002-2205-8305
Madarina Julia http://orcid.org/0000-0001-8847-2050
Dian Caturini Sulistyoningrum http://orcid.org/0000-0001-9654-2151
Poh Bee Koon http://orcid.org/0000-0003-0713-5197
Margaret Danchin http://orcid.org/0000-0002-7624-5691
Indah Kartika Murni http://orcid.org/0000-0001-9174-8425

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