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Association between 25-Hydroxyvitamin D and Mental-Emotional Status in Children during Their First 1,000 Days of Life

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Abstract

Vitamin D receptors are widely expressed in brain tissue, including in the limbic system that plays a role in children's mental and emotional development. This study aimed to analyze the relationship between 25-(OH)-D level and children's mental-emotional development during their first 1000 days of life. A cross-sectional study was conducted on children aged ≤2 years old in Waled and Sukabumi regions using secondary data from previous cohort investigations entitled "The Role of Vitamin D in Efforts to Reduce Maternal and Infant mortality". The measurement of 25-(OH)-D concentration and assessment of the mental-emotional development were performed using the Ages and Stages Questionnaires: Social-Emotional (ASQ-SE) questionnaire. Other child and maternal characteristics, and several laboratory results, were also obtained. Statistical analyses were performed using the Spearman rank, Pearson correlation test, and multivariate linear regression analysis. A total of ninety-two children were included, and the median vitamin D level of the population was 20.17 ng/mL (IQR 4.43–49.97). The correlation analysis showed that no significant relationship between children's mental-emotional scores and the parameters tested, including the concentration of 25-(OH)-D (correlation coefficient 0.08; p=0.446). There was no relationship between the vitamin D concentration and mental-emotional development. Based on these results, it is concluded that there is no correlation between 25-(OH)-D concentration and children's mental-emotional development during the first 1000 days of life. However, further investigations are recommended to eliminate various confounding factors.

Keywords: Infant, mental-emotional, maternal education, vitamin D

Introduction

The first 1,000 days of life, which are from conception to the age of 2, are critical for a child's mental and emotional development. During this time, there is an increase in the number of brain neurons and synapse formation that serves as the foundation for subsequent developmental processes such as mental and emotional development.[1–3] A successful mental-emotional development will lead to children who are mentally and emotionally healthy, have a positive quality of life and socialize well at home, school, as well as in the community. In children, mental health implies that a child can reach developmental and emotional maturity stages, learn and build healthy social relationships, and understand how to deal with problems. Meanwhile, emotional health is the ability to manage and express feelings as well as emotions in an age-appropriate manner.[4,5] Disturbances during the first 1,000 days of life period will impair the child's quality of life. According to WHO, 10–20% of children and adolescents globally suffer from mental-emotional and behavioral disorders, which affect younger and older children, respectively.[6,7]

The interaction of genetic and environmental factors influences mental and emotional development, one of which is optimal nutritional intake.[5,8,9]including disruptive, depression, anxiety and pervasive developmental (autism Investigations have shown that vitamin D is important for bone growth as well as calcium homeostasis regulation and plays a role in brain development, cell differentiation, axonal growth, neurotrophic factor stimulation, anti-

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inflammatory effects, and the production of free radicals from the brain. The vitamin D metabolic product, namely 1,25-dihydroxy vitamin D (calcitriol) is a secosteroid hormone that regulates many genes.[9,10] Furthermore, its receptors are widely expressed in brain tissue, including the limbic system, and play a role in children's mental and emotional development.[11]there has been a lack of direct evidence about its role in the human brain. This paper reports, for the first time, the distribution of the 1,25-dihydroxyvitamin D 3 receptor (VDR Although previous reports yielded different results with some concluding that there is a relationship,[12–14] others stated that there is no significant correlation between vitamin D levels and children's mental-emotional development.[15] Studies involving children in their first 1000 days of life are still uncommon and no research has used the ASQ-SE questionnaire method.[9,16] The Indonesian version of the Ages & Stages Questionnaires®: Social-Emotional (ASQ:SE) screening test can now be administered to children aged 12–36 months. This is because it met the validity criteria and has fairly good reliability, according to Cesilia et al.[17] Therefore, this study aims to analyze the relationship between 25-(OH)-D levels and children's mental-emotional development at the first 1,000 days of life using the ASQ-SE questionnaire.

Methods

A cross-sectional correlative analytical study was carried out using secondary data from a previous cohort investigation conducted in the Waled and Sukabumi regions of West Java, Indonesia in 2019. The subjects were healthy 2-year-old children, who were previously enrolled in the Academic Leadership Grant cohort study "The Role of Vitamin D in Efforts to Reduce Maternal and Infant Mortality Rates". Informed consent from both children and parents was obtained before the study. Ethical approval was obtained from the Ethical Committee for Health Research, Universitas Padjadjaran, West Java, Indonesia with registration 335/UN6/KEP/EC/2018. Inclusion criteria are every child in the previous cohort study who had complete data, while the exclusion criteria are born prematurely, had low birth weight, and had comorbidities.

Consecutive sampling was used to select the study subjects. The sample size was calculated using a 95% confidence interval (CI) and 80% power test, as well as the significant correlation coefficient of the relationship between children's vitamin D levels and mental-emotional development status at r = -0.36, leading to a minimum size of 59 children. Vitamin D concentration and ASQ-SE score data were obtained from the previous cohort study. When the child was 2 years old, 25-(OH)-D levels were measured in blood samples, and the child's mental as well as emotional development was assessed by doctors, nurses, or midwives who had been trained to use the ASQ-SE questionnaire. Other variables of children's characteristics including gender, anthropometric measurements, nutritional status, and maternal variables including age, educational level, and occupation were collected. Several laboratory examination results were also obtained such as serum levels of hemoglobin, iron, zinc, and folic acid. Subsequently, the laboratory examination was carried out in Biomedical Laboratory Medical Faculty, Universitas Padjadjaran.

Vitamin D concentrations were measured using the enzyme-linked fluorescent assay (ELFA; VIDAS®) method and expressed as ng/mL. Ages and Stages Questionnaires: Social Emotional (ASQ-SE) was used to monitor a child's development in the behavioral areas of self-regulation, compliance, communication, adaptive behavior, autonomy, affect, and interaction with people. This questionnaire has been validated in the Indonesian version. Parents can answer each question with the choice of "Most of the Time" (0 points), "Sometimes" (5 points), "Rarely or Never" (10 points), and "Checked concern" (5 additional points). The maximum number of points that can be earned for each item is 15. A child's nutritional status is declared as undernourished when the child was found to be wasted (weight-for-height Z-Score <-2SD according to the WHO growth curve) or stunted (height-for-age Z-Score <-2SD), and normal when Z scores of weight-for-height and height-for-age were between -2 SD to +2 SD.

Categorical data were presented as numbers and percentages, while continuous data were shown as mean and standard deviation (SD) or median (IQR). To examine the relationship between two variables, correlation analysis was performed using the Pearson or Rank Spearman correlation test. The data distribution of hemoglobin and vitamin D concentration, as well as mental-emotional scores, were normal, while other variables have abnormal. The relationship between vitamin D levels and mental-emotional development (ASQ-SE) was studied using multivariate linear regression analysis, with

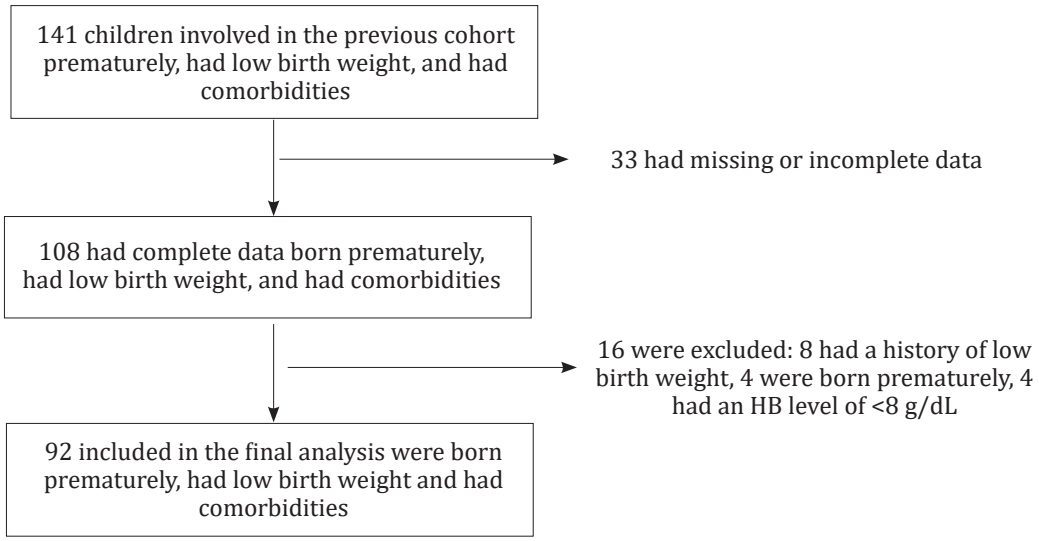

Figure Study Flowchart

confounding variables including parental education level and occupation, nutritional status, hemoglobin, zinc, folic acid, and iron level. The p-value of ≤0.05 was used to determine the significance of the test results.

Table 1 Characteristics of Study Subjects

Characteristics	n (%)	Median (IQR)
Gender		
Boys	41 (45)	
Girls	51 (55)	
Anthropometric measure		
Body weight (kg)		11,0 (8–16)
Body length (cm)		85,0 (77–92)
Head circumference (cm)		46,0 (43–51)
Nutritional status		
Normal	70 (76)	
Undernutrition	22 (24)	
Maternal age (years)		28,0 (18–40)
Maternal education		
≤ Junior High School	71 (77)	
≥ Senior High School	21 (23)	
Maternal occupation		
None	77 (84)	
Work	15 (16)	

Results

A total of 141 children were involved in the previous cohort study and only 108 had complete data. Meanwhile, 16 children were excluded, where 8 had a history of low birth weight, 4 were born prematurely, and 4 had a Hb level of <8 g/dL as shown in Figure. A total of 41 (45%) children were boys, 70 children (76%) had good nutritional status, while 22 (24%) had poor nutrition. From the maternal characteristics shown in Table 1, 77% had a junior high school education or less and 84% did not work. Laboratory examination results are listed in Table 2.

The correlation analysis revealed that there was no statistically significant relationship between children's mental-emotional scores and the parameters studied (p>0, 05), including maternal age, Hb levels, zinc levels, iron levels, folate levels, and vitamin 25-(OH)-D levels (Table 3).

Table 4 shows the differences in children's vitamin 2-5(OH)-D levels and mental-emotional scores based on various parameters. It was discovered that vitamin 25-(OH)-D levels were higher in mothers with a higher level of education and those who did not work. A statistically significant parameter for children's mental-emotional development scores is maternal education, mothers with at least a senior high school education level had children with lower emotional development scores, indicating better emotional development.

Table 2 Laboratory Examination Results

Variables	Statistical Measure			
	Mean	SD	Median	IQR
Hb (g/dl)	11.21	1.42	11.4	8.3–13.7
Zinc	3.70	2.70	2.9	1.1–16.4
Iron	5.61	7.78	3.00	1–47
Folic acid	93.29	73.4	77.2	8.7–489.2
Vitamin D	20.69	9.24	20.17	4.43–49.97
Emotional mental score	54.67	26.04	50	5–120

Table 3 Correlation Analysis between Children's Mental-Emotional Scores with Various Parameters

Parameters	Correlation coefficient (r)	P value
Maternal age	-0.023	0.826
Hb levels	-0.171	0.105
Zinc levels	0.074	0.485
Iron levels	0.007	0.947
Folic acid levels	0.047	0.659
Vitamin D levels	0.080	0.446

Notes: r=Spearman rank correlation coefficient was used, except Hb levels and Vitamin D levels, which were tested using the Pearson correlation test due to the normal distribution of data

Multiple linear regression analysis was conducted to analyze the factors that were multivariable and associated with the children's mental-emotional score at the age of 2 years. The variables included have a p-value of <0.25 based on the results of bivariable analysis, namely maternal education, hemoglobin levels, and nutritional status. Although not statistically significant, vitamin D levels were included. The results revealed that the mother's education level was inversely proportional to the child's mental-emotional development score. This indicated that the higher the mother's education level, the better the child's mental-emotional development (R^2=8.6%) (Table 5).

Discussion

This study provides information about the relationship between vitamin D levels and the mental-emotional development of children at the age of 2 years using the ASQ-SE questionnaire. The first 1,000 days of life were chosen because, during this period, the growth of brain cells and nerve fibers occurs most rapidly, which makes it crucial for the emotional and mental development of children.[1–3] The Indonesian version of the ASQ-SE questionnaire used has passed the validity and reliability test for children

Table 4 Comparison of Vitamin D Levels and Mental-Emotional Scores by Various Parameters

Parameters	Vitamin D levels		Mental-emotional Scores	
	Statistical Measure	P Value*	Statistical Measure	P Value*
Gender:				
Boys	22.35 (7.75–49.97)	0.062	55 (15–105)	0.573
Girls	18.0 (4.43–44.9)		50 (5–120)	
Nutritional status:				
Normal	20.2 (7.25–49.97)	0.840	50 (5–120)	0.105
Undernutrition	18.95 (4.43–44.99)		57.5 (15–110)	
Maternal education:				
≤Junior High School	18.35 (4.43–44.99)	0.044	55 (15–120)	0.004
≥Senior High School	24.6 (7.75–49.97)		40 (5–90)	
Maternal occupation:				
None	20.42(4.43–49.97)	0.012	50 (5–120)	0.564
Work	12.53 (7.25–36.47)		50 (15–95)	

Notes: data is presented with the median value (IQR); *) Mann-Whitney test

Table 5 Multiple Linear Regression Analysis

Variables	B Coeff	SE (B)	T	P Value
Initial model:				
Vitamin 25-(OH)-D levels	0.492	0.290	1.696	0.094
Hb levels	-2.101	1.942	-1.082	0.282
Nutritional status	-4.304	6.241	-0.690	0.492
Maternal education	-17.655	6.460	-2.733	0.008
Final model:				
Maternal education	-17.810	8.009	-2.893	0.005
Constant	75.095	-	-	

Note: for the initial model R^2 (%)=13.1% (R=0.362); for the final model R^2 (%)=8.6% (R=0.293)

aged 24 months. The results showed that there was no correlation between vitamin D levels and children's mental-emotional development scores, with a correlation coefficient of 0.08 and a p-value of 0.446.

These results are similar to the study conducted on older children, with a mean age of 9.9 years in the UK by Tolppanen et al.,[15] where the SDQ (Strengths and Difficulties Questionnaire) screening test was used. It was discovered that there is no significant relationship between serum 25-(OH)-D3 and 25-(OH)-D2 concentrations with behavioral disorders in children, where the fully adjusted odds ratio: OR with 95% confidence interval: CI was 0.85 (0.74, 0.98). However, other reports showed the statistical significance of the association between vitamin D levels and children's mental and emotional development. Tofail et al.,[12] who involved 265 children aged 6-8 months in the slum area of Bangladesh, reported a significant relationship between vitamin D deficiency and child behavior scores assessed using the Bailey-III screening test. Higher levels of vitamin D in these infants showed a positive association with temperament, language, and behavior but not with cognitive and motor development. Karabel et al.[13] carried out an investigation involving 138 adolescents with depression. The results showed that there was a negative correlation between vitamin D levels and patients' depression scores, where children with vitamin D deficiency were more likely to experience depressive symptoms than those with normal levels (r=-0.368, P= 0.03). Husmann et al.[14] Vitamin D has been hypothesized to play a role in brain development and cell differentiation, axonal growth, neurotrophic factor stimulation, anti-inflammatory effects, and modulating the production of brain-derived free radicals.[9,10] Furthermore, Vitamin D receptor (VDR) and 25-hydroxyvitamin D3 1-alpha-hydroxylase have also been found in brain tissue, particularly in the hypothalamus and substantia nigra, confirming its brain function, including in terms of mental-emotional regulation.[11]

The lack of statistical significance in this study can be attributed to the absence of data about other potential factors in the analysis. Parenting patterns are one of the factors that can have an impact on mental-emotional development but were not investigated. This is because the nurturing environment and parenting patterns play an important role in shaping a healthy state in children.[11] According to an investigation by Ghozali et al.[18] which involved children aged 3–5 years in Qatar, children raised with authoritative parenting patterns had better personal and social development than those with permissive parenting.Similarly, Haslam et al. discovered that children aged 2–10 years in Australia and Indonesia with authoritative parenting had better emotional regulation and experienced fewer behavioral disturbances compared to those with authoritarian parenting.[19] Other factors that may contribute to a child's mental-emotional development include the family's socioeconomic status, the mental health of the parents, and the state of family harmony.[20–24] These various factors of the relationship between children and their parents/guardians as well as a good parenting environment have a positive impact on the mental and emotional development of children, although genetic and environmental risk factors are obtained concurrently.[20,25] When other external risk factors such as poor nutrition are obtained, but the child grows up in a family environment that supports his mental-emotional development, the risk of mental-emotional disorders is reduced.[20,26] This can be considered as the cause of the inability

to discover a significant correlation between vitamin D levels and children's mental and emotional development scores in this study.

This study also observed other factors that might influence children's mental and emotional development such as nutrient intake other than vitamin D, children's nutritional status, maternal education, and occupation. The final model from the multivariate analysis showed that only maternal education level had a significant impact on children's mental and emotional development. This is because mothers with a higher educational level have a better understanding. They also have a better perception of the parental roles in their children's education and an understanding of a good parenting model. This is in line with the study by Fauziyah et al. conducted at 4 Community Health Centers, Sidoarjo District, East Java, and involved 120 preschool children. The results showed that mental and emotional development was directly affected by the authoritative parenting style (b=4.81, 95% CI= 3.05 to 6.56, p=<0.001), and the authoritative parenting style was positively affected by maternal education level ≥senior high school (b=2.14, 95% CI= 0.03 to 4.24, p=0.046). It was also discovered that maternal education was associated with family income, which indirectly affects the children's mental and emotional development.[27]

The limitation of this study is the use of secondary data, leading to the inability to obtain more data on other factors that can also affect the children's mental and emotional development in early childhood, such as parenting patterns, family socioeconomic conditions, and children's relationships with caregiver or siblings. The possibility of different parenting patterns, family conditions, and the heterogeneous characteristics of the subjects will have an effect and limit the generalizability of the results to the entire population. Further investigation is required to assess the validity, replicability, and generalizability of this study. Furthermore, there is no cut-off point for vitamin D concentration for populations in tropical countries like Indonesia.

In conclusion, this study does not support the hypothesis that there is a relationship between vitamin D levels and children's mental and emotional development in the first 1,000 days of life. This is because the only factor that had a significant impact was maternal education. Therefore, further study using primary data with a larger sample size and more homogenous subjects is required. It is also necessary to investigate other parameters such as parenting models and family harmony, which are important factors in children's mental and emotional development.

References

1. Cusick S, Georgieff MK. The first 1,000 days of life: the brain's window of opportunity [Internet]. UNICEF Office of Research-Innocenti. 2013 [cited 2017 Mar 29]. Available from: https://www.unicef-irc.org/article/958-the-first-1000-days-of-life-the-brains-window-of-opportunity.html
2. Martorell R. Improved nutrition in the first 1000 days and adult human capital and health. Am J Hum Biol. 2017;29(2):1–24.
3. Schwarzenberg SJ, Georgieff MK. Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. Pediatrics. 2018;141(2):e20173716.
4. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington: American Psychiatric Publishing; 2016.
5. Ogundele MO. Behavioural and emotional disorders in childhood: A brief overview for paediatricians. World J Clin Pediatr. 2018;7(1):9–26.
6. World Health Organization. Adolescents and mental health [Internet]. 2017 [cited 2020 Jan 15]. Available from: https://www.who.int/maternal_child_adolescent/topics/adolescence/mental_health/en.
7. Cree RA, Bitsko RH, Robinson LR, Holbrook JR, Danielson ML, Smith C, et al. Health care, family, and community factors associated with mental, behavioral, and developmental disorders and poverty among children aged 2–8 years-United States, 2016. MMWR Morb Mortal Wkly Rep. 2018;67(50):1377–83.
8. Clinton J, Feller AF, Williams RC. The importance of infant mental health. Paediatr Child Health. 2016;21(5):239–41.
9. Mutua AM, Mogire RM, Elliott AM, Williams TN, Webb EL, Abubakar A, et al. Effects of vitamin D deficiency on neurobehavioural outcomes in children: a systematic review. Wellcome Open Res. 2020;5:1–27.
10. Sassi F, Tamone C, D'amelio P. Vitamin D: Nutrient, hormone, and immunomodulator. Nutrients. 2018;10(11):1–14.
11. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ. Distribution of the Vitamin D receptor and 1α-hydroxylase in human brain. J Chem Neuroanat. 2005;29(1):21–30.

12. Tofail F, Munirul Islam M, Mahfuz M, Ashraful Alam M, Aktar S, Haque R, et al. Association of vitamin D nutrition with neurodevelopmental outcome of infants of slums in Bangladesh. PLoS One. 2019;14(9):1–15.
13. Karabel M, Şimsek Ş, Kenan Haspolat Y, Kelekçi S, Karabel D, Tuncel T, et al. The association between depression and vitamin D and parathyroid hormone levels in adolescents. Int J Pediatr. 2016;4(2):1365–72.
14. Husmann C, Frank M, Schmidt B, Jöckel KH, Antel J, Reissner V, et al. Low 25(OH)-vitamin D concentrations are associated with emotional and behavioral problems in German children and adolescents. PLoS One. 2017;12(8):1–16.
15. Tolppanen AM, Sayers A, Fraser WD, Lewis G, Zammit S, Lawlor DA. The association of 25-hydroxyvitamin D3 and D2 with behavioural problems in childhood. PLoS One. 2012;7(7):1–8.
16. Głąbska D, Kołota A, Lachowicz K, Skolmowska D, Stachoń M, Guzek D. The influence of vitamin d intake and status on mental health in children: A systematic review. Nutrients. 2021;13(3):1–22.
17. Cesilia C, Diah Asri Wulandari, Dhamayanti M. Validitas dan reliabilitas ages & stages questionnaire: social-emotional 2 versi Indonesia. Sari Pediatr. 2021;22(6):343–50.
18. Ghozali S. The influence of parenting patterns on the personal social development of preschool children. South East Asia Nurs Res. 2020;2(2):70–3.
19. Haslam D, Poniman C, Filus A, Sumargi A, Boediman L. Parenting style, child emotion regulation and behavioral problems: the moderating role of cultural values in Australia and Indonesia. Marriage Fam Rev. 2020;56(4):320–42.
20. Hosokawa R, Katsura T. Effect of socioeconomic status on behavioral problems from preschool to early elementary school-A Japanese longitudinal study. PLoS One. 2018;13(5):1–23.
21. Arroyo-Borrell E, Renart G, Saurina C, Saez M. Influence maternal background has on children's mental health. Int J Equity Health. 2017;16(63):1–10.
22. Vukojević M, Zovko A, Talić I, Tanović M, Rešić B, Vrdoljak I, et al. Parental socioeconomic status as a predictor of physical and mental health outcomes in children-Literature review. Acta Clin Croat. 2017;56(4):742–8.
23. Hattangadi N, Cost KT, Birken CS, Borkhoff CM, Maguire JL, Szatmari P, et al. Parenting stress during infancy is a risk factor for mental health problems in 3-year-old children. BMC Public Health. 2020;20(1726):1–7.
24. Schaan VK, Schulz A, Schächinger H, Vögele C. Parental divorce is associated with an increased risk to develop mental disorders in women. J Affect Disord. 2019;257:91–9.
25. Pinquart M. Associations of parenting dimensions and styles with externalizing problems of children and adolescents: An updated meta-analysis. Dev Psychol. 2017;53(5):873–932.
26. Zeanah CHJ, Zeanah PD. The Scope of Infant Mental Health. In: Zeanah CH, editor. Handbook of Infant Mental Health. 3rd ed. Guilford Press; 2011. p. 5–21.
27. Fauziyah R, Salimo H, Murti B. Influence of psycho-socio-economic factors, parenting style, and sibling rivalry, on mental and emotional development of preschool children in Sidoarjo District. J Matern Child Heal. 2017;2(3):233–44.