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Association between 25-hydroxyvitamin D levels and incidence of allergy and infection in infants aged 0–6 months

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ABSTRACT

Introduction: Vitamin D levels are known to be related to prevalence of allergy and infection in children. However, vitamin D levels in infants' umbilical cord blood need to be investigated. Therefore, this study aimed to determine association between 25-hydroxyvitamin D [25(OH)D] levels and incidence of allergy and infection in children. **Methods:** A longitudinal study involving 38 full-term newborns was conducted. Serum 25(OH)D levels in infants' umbilical cord and venous blood were measured at birth and six months, respectively. 25(OH)D levels were classified as insufficient (<20 ng/mL) and sufficient (>20 ng/mL). Parents filled out questionnaires about their children's allergy and infection symptoms. Paired *t*-test was performed to compare the 25(OH)D levels at birth and at six months. Chi-squared test was conducted to determine relationship between 25(OH)D levels and incidence of infection and allergy in children. **Results:** 25(OH)D levels in venous blood of 6-month-old infants were significantly higher than in umbilical cord blood (50.44±13.59 ng/mL vs. 20.70±6.60 ng/mL, $p<0.001$). In addition, 25(OH)D level insufficiency in umbilical cord blood was associated with infection ($p<0.05$). However, there was no incidence of allergy, and exclusive breastfeeding and sun exposure were not associated with vitamin D levels in 6-month-old infants. **Conclusion:** We conclude that 25(OH)D level insufficiency in umbilical cord blood was associated with incidence of infection in the first six months of life.

Keywords: 25(OH)D, allergy, infants, infection, umbilical cord blood

INTRODUCTION

Vitamin D and calcium deficiencies are widespread, making them global health concerns, particularly for infants, children, and adolescents (Amrein *et al.*, 2020). A systematic review in the South-East Asia region showed that vitamin D deficiency among healthy children is common. Its prevalence ranges from 0.9% to 96.4%, with >50% of newborns suffering from vitamin D deficiency (Oktaria *et al.,* 2022). Data from Yogyakarta, Indonesia, revealed that vitamin D deficiency was detected in 90% of umbilical cord blood samples and 13% of venous blood samples obtained from 6-month-old infants (Oktaria *et al.*, 2020).

It has been hypothesised that vitamin D deficiency is related to acute and

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chronic diseases, including infectious diseases, allergies, autoimmune and neurological disorders, dental caries, cardiovascular disease, type 2 diabetes, and cancer (Holick, 2017). The role of vitamin D in modulating the immune system against various pathogens is through cathelicidin, which activates autophagy and enhances antimicrobial function against pathogens and inflammation (Chung *et al.*, 2020).

Allergic diseases are relatively common in developed countries, affecting four to five individuals (Wang, 2011). A study conducted on a group of patients aged 0–18 years with atopic dermatitis, asthma, and food allergies demonstrated that 48% of them had insufficient serum 25-hydroxyvitamin D [25(OH)D] levels (<30 ng/mL) (Searing & Leung, 2010). In addition, a study conducted in Taiwan showed that low serum 25(OH) D level in the umbilical cord blood was associated with a high risk of respiratory tract infection in infants aged below six months (Lai *et al.*, 2017).

The correlation between vitamin D levels in umbilical cord blood and allergic and infectious diseases has yet to be adequately investigated in Indonesia. Therefore, this study aimed to determine the association between serum 25(OH) D level in the umbilical cord blood and the incidence of allergy and infection in the first six months of life. Further, it aimed to analyse the difference between serum 25(OH)D levels in umbilical cord blood and in venous blood, as well as the effect of exclusive breastfeeding and sun exposure on serum 25(OH)D levels.

MATERIALS AND METHODS

Study design

This longitudinal study was conducted in Semarang, Central Java, Indonesia, from May 2017 to August 2018. The inclusion criteria for the infants were full-term, singleton, vigorous, and without a history of asphyxia. Meanwhile, the inclusion criteria for the mothers were age <40 years, no pregnancy complications, and willingness to participate in the study from the third trimester until the first six months post-delivery. Sample size was calculated by comparing two proportions formula (Wang & Chow, 2007), with confidence level of 95%, α=0.05, critical value of 1.96, and power=80%. With p1 and p2 as the expected sample proportions of the two groups, the minimum sample calculated was 35 subjects.

All subjects were asked for written informed consent. Umbilical cord blood samples of 50 infants were obtained from hospitals and primary health care centres. During the study period, several infants were excluded: three, who stopped study participation; eight, whose parents refused blood collection; and one, who died. Thus, only 38 infants (22 boys and 16 girls) were included in the final analysis. However, the required minimum sample size was still met. The protocol for this study was approved by the Faculty of Medicine, Diponegoro University ethics committee (Approval no.: 18/EC/FK-RSDK/I/2017).

Allergic and infectious diseases

Allergic manifestations in the gastrointestinal tract (diarrhoea), skin (atopic dermatitis, eczema, urticaria, and angioedema), and respiratory tract (wheezing, nasal hypersecretion, bronchial hypersecretion) were obtained from the questionnaires the parents had answered. In addition, infections consisting of fever with symptoms in the respiratory tract, gastrointestinal tract (diarrhoea), and skin infection were reported by parents in the questionnaires.

Breastfeeding

Exclusive breastfeeding was defined

as feeding an infant with breast milk without any additional food/drink, not even water (WHO and UNICEF, 2021).

Sun exposure

The length of sun exposure was calculated in minutes/week. The infants were exposed to the sun wearing minimal clothing (>50% exposure) and with no sun protection, such as umbrellas, shades, and sunblock, at 8 to 10 a.m. in the morning. The length of sun exposure was categorised as >30 minutes/week and <30 minutes/week, and the exposure was evaluated for six months (Anusha *et al.*, 2019).

Blood samples

Blood sample was collected from the umbilical cord after the infant was born, before the placenta was taken away. Blood (3 mL) was taken by placing two clamps of 10±15 cm on the umbilical cord. Blood from the umbilical vein was collected using a 5-mL syringe and then injected into a non-ethylenediamine tetra acetic acid tube. Blood samples of the 6-month-old infants were obtained from the vein. All samples were brought to the Dr. Kariadi Hospital, Semarang, Indonesia. Samples were centrifuged at 3000 rpm for 10 minutes, and the serum was separated and stored in a freezer at -20°C. After the specimen was collected using a packed cold chain method and stored in a cool box, it was delivered to the GAKI Laboratory of Diponegoro National Hospital, Semarang, Indonesia for the analysis of 25(OH)D level.

Serum 25(OH) D analysis

The serum 25(OH)D levels at birth (from the umbilical cord blood) and six months of age were measured via enzyme-linked immunosorbent assay and using the ELX-800 microplate reader (BioTek Instruments, Inc., Winooski, USA). The 25(OH)D levels were categorised as sufficient (>20 ng/mL or >50 nmol/L) and insufficient (≤20 ng/mL or ≤50 nmol/L) (Amrein *et al.*, 2020).

Data calculation and statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows version 25.0 (IBM Corporation, Armonk, New York, USA). A normality test was conducted to determine the distribution of numeric variables before analysis. Normally distributed numeric variables were expressed as mean (standard deviation), whereas non-normally distributed ones were expressed as median (minimum and maximum). Categorical variables were presented in a frequency distribution. The difference between serum 25(OH)D levels in umbilical cord blood of newborns and serum 25(OH)D levels in venous blood of 6-month-old infants was evaluated using paired *t*-test. Chi-squared test was employed to analyse the association between 25(OH)D levels with allergic and infectious diseases in infants up to six months old.

RESULTS

The characteristics of the infants were as follows: 26 (68.4%) were born through normal deliveries, 18 (47.4%) were exclusively breastfed (EBF), 36 (94.7%) were exposed to the sun for more than 30 minutes/week, and all infants received complete immunisations according to their age.

Mean 25(OH)D levels in the umbilical cord blood and venous blood of 6-month-old infants are presented in Table 1. Of the 38 umbilical cord blood samples, 50% were found to have sufficient 25(OH) D levels, whereas 50% had insufficient 25(OH)D levels. Contrarily, all samples from 6-month-old infants had sufficient 25(OH)D levels. Furthermore, the 25(OH) D levels in venous blood of 6-month-old infants were also higher than those

Table 1. Comparison of 25(OH)D levels in the umbilical cord blood and at six months

Vitamin D level	*n*	25(OH)D level *(Mean±SD)*	*p*
Umbilical cord blood (ng/mL)	38	20.70±6.60	<0.001†*
6 months (ng/mL)	38	50.44±13.59	

†Paired *t*-test
*Significance, $p<0.05$

Table 2. Association between insufficient 25(OH)D levels in the umbilical cord blood and infection

	25(OH)D insufficient n (%)	*25(OH)D sufficient n (%)*	*p*
Infections (URI and diarrhoea)			
Yes	10 (71.4)	4 (28.6)	0.044†*
No	9 (37.5)	15 (62.5)	
URI			
Yes	8 (66.7)	4 (33.3)	0.163†
No	11 (42.3)	15 (57.7)	
Diarrhoea			
Yes	2 (100.0)	0 (0.0)	0.486‡
No	17 (47.2)	19 (52.8)	

URI: upper respiratory infection
†Pearson's chi-squared test
‡Fisher's exact test
*Significance, $p<0.05$

Table 3. Comparison of 25(OH)D levels (ng/mL) among 6-month-old infants according to breastfeeding status and sunlight exposure

Variables	*n*	25(OH)D level *(Mean±SD)*	*p*
Exclusively breastfed	18	48.52±9.52	0.406†
Non-exclusively breastfed	20	52.16±16.50	
Sunlight exposure			
>30 min/week	36	51.00±13.53	0.283†
<30 min/week	2	40.80±14.89	

†*t*-test

of newborns (20.70±6.60 ng/mL vs. 50.44±13.59 ng/mL, $p<0.001$) (Table 1).

There were no reports of infants experiencing allergic symptoms, but seven infants (18.4%) had a family history of allergy. Infectious diseases, such as upper respiratory infection (URI) and diarrhoea, occurred in 14 infants, of whom 10 had insufficient 25(OH)D levels in the umbilical cord blood (Table 2). However, no skin infection occurred in the infants and none of them were hospitalised. In addition, a significant association was observed between insufficient 25(OH)D levels in the umbilical cord blood and infection.

However, there was no significant association between 25(OH)D levels in the umbilical cord blood and URI or diarrhoea *per se* (Table 2).

Although the 25(OH)D levels of EBF infants were lower than those of non-EBF infants at six months of age, the 25(OH)D levels were higher in those who were exposed to the sun for more than 30 minutes/week than in those who were exposed for less than 30 minutes/week; however, the differences were not statistically significant (Table 3).

DISCUSSION

In this study, the 25(OH)D levels in the umbilical cord blood of 19 infants (50%) were insufficient. This finding is consistent with that from a previous study on South-East Asian newborns, which indicated that 20.2% of newborns were categorised as vitamin D deficient (<12 ng/mL) and 69.1% as vitamin D insufficient (12–20 ng/mL) (Ariyawatkul & Lersbuasin, 2018). A meta-analysis revealed that vitamin D deficiency in Turkey varied from 58.9% to 66.6% and that the risk was higher among neonates, pregnant women, and adult women. It also showed that 86.6% of infants had vitamin D deficiency (Alpdemir & Alpdemir, 2019). Infants born to mothers of non-white race/ethnicity have a higher risk of vitamin D deficiency (Eldjerou *et al.*, 2015). Mean 25(OH)D levels in 100 umbilical cord blood samples according to maternal ethnicity were reportedly higher in Caucasians than in Asians, Hispanics, Pacific Islanders, and African Americans (Halm *et al.*, 2013).

This study found that EBF infants had lower vitamin D levels at six months old than non-exclusively breastfed infants. However, both groups still had sufficient vitamin D levels (>20 ng/mL). This finding is inconsistent with that from a study conducted in Indonesia, which indicated that EBF infants were twice as likely to have vitamin D deficiency at six months of age (Oktaria *et al.*, 2020). Furthermore, a significant difference in the vitamin D levels between newborns and 6-month-old infants was observed (p<0.001). A previous study in Denmark reported that 4-month-old infants had vitamin D levels of 94.1±24.2 nmol/L, whereas 9-month-old infants had 82.2±18.9 nmol/L; more than 90% of the infants received vitamin D supplementation (Streym *et al.*, 2013). Contrarily, a study in South Korea reported that vitamin D deficiency (<20 ng/mL) occurred in 48.7% of infants aged 1–6 months. It also showed that the most significant risk factor was exclusive breastfeeding (Choi, Kim & Jeong, 2013). Breast milk and formula milk contain a very small amount of vitamin D. Breast milk contains only <20 IU/L of vitamin D and even less if the mother has low exposure to the sun, which is insufficient to meet the infant's growing needs. Thus, without fortification, EBF infants will receive <20% of their daily needs (Ruangkit *et al.*, 2021). 25(OH)D concentration is found to be higher in hindmilk than in foremilk [2.10% (1.63%–2.65%) vs. 1.35% (1.04%–1.84%), respectively]. 25(OH)D concentration in breast milk is also correlated with maternal plasma concentration; mothers who received vitamin D supplementation have higher 25(OH)D concentrations in their breast milk than those who did not (Streym *et al.*, 2016).

In our study, neither the vitamin D insufficient group nor the vitamin D sufficient group reported any incidence of allergic diseases. This finding is in line with that from a study in Australia, which administered 400 IU of vitamin D supplementation to children aged 1–2.5 years who had familial history of allergy; the results indicated that vitamin D supplementation did not reduce the

development of allergies (Rueter *et al.*, 2020). Another study conducted on children with persistent asthma and vitamin D deficiency found no clinical differences in asthma attacks between the experimental and control groups (Forno *et al.*, 2020).

A significant association was observed between insufficient 25(OH) D levels in the umbilical cord blood and infection. A study on 122 infants in Taiwan found that a serum 25(OH)D level below 13.7 ng/mL in the umbilical cord blood was correlated with a higher risk of respiratory tract infection before the infants reached six months old (Lai *et al.*, 2017). Furthermore, it was reported that infants with a low 25(OH)D level had a higher risk of respiratory tract infection before reaching three months old (Camargo *et al.*, 2011). Similarly, our study demonstrated that infants with insufficient 25(OH)D levels in the umbilical cord blood had a 4.2 times higher risk of URI. Similar results were obtained from a study in Saudi Arabia, whereby low 25(OH)D levels in the umbilical cord blood also increased the risk of lower respiratory tract infection in children at two years of age (Mohamed & Al-Shehri, 2013). Another study in Indonesia found that 19% of infants and children with pneumonia had vitamin D deficiency; however, it was not related to the severity of pneumonia (Oktaria *et al.*, 2021).

A previous study in Tanzania reported that the prevalence rates of vitamin D deficiency and insufficiency in 188 children aged <5 years were relatively high, at 53.7% and 34%, respectively; however, no association was observed between vitamin D level and the incidence of diarrhoea (Hassam *et al.*, 2019). Similarly, our study found no association between the incidence of diarrhoea and insufficient 25(OH)D levels in the umbilical cord blood, with just two of our infants having diarrhoea.

Despite the sun being the main source of vitamin D, there are concerns regarding excessive sun exposure as one of the risk factors for skin cancer. The American Academy of Pediatrics recommends that infants below the age of six months not be exposed to direct sunlight (Long, 2017). In this study, data about infants' sun exposure were obtained. We found that 6-month-old infants with sun exposure <30 minutes/ week and those with sun exposure >30 minutes/week had sufficient vitamin D levels (>20 ng/mL). This finding is supported by a study in Sri Lanka, which reported that sun exposure >30 minutes/week was significantly associated with higher vitamin D levels in infants aged 4–6 weeks (Anusha *et al.*, 2019). In addition, a study in India also reported that sun exposure of at least 30 minutes/week for at least 16 weeks achieved sufficient vitamin D levels (>20 ng/mL) in 6-month-old infants (Meena *et al.*, 2017). Our data indicated that 94.7% of infants received sun exposure >30 minutes/week.

A study on sun exposure in South-East Asia has reported that the highest intensity of ultraviolet B is from 10 a.m. to 3 p.m., when the sun is directly above the head. A previous study conducted in Semarang, Indonesia, on 109 infants aged 7–12 months has reported that sun exposure from 10 a.m. to 2 p.m., three times per week for 5 minutes (50% of body surface area) for two months, can increase serum 25(OH)D levels by 8.9 ng/mL (Pratiwi, 2019).

The limitations of this study were that several parents refused to allow their child's blood to be taken at six months of age, and vitamin D levels in the mothers' blood were not measured. However, to the best of our knowledge, this is the first study in Indonesia that has analysed the association of vitamin D levels in the venous blood and umbilical cord blood of 6-month-old infants with

the incidence of allergic and infectious diseases.

CONCLUSION

The incidence rate of 25(OH)D level insufficiency in the umbilical cord blood was 50%. The 25(OH)D level in the venous blood of 6-month-old infants was higher than that in the umbilical cord blood of newborns. Significant association was observed between 25(OH)D level insufficiency in the umbilical cord blood and infection. However, allergic diseases did not occur in both the insufficient and sufficient 25(OH)D groups. Further study is needed to analyse the vitamin D levels of infants diagnosed with allergic and infectious diseases.

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Authors' contributions

Mexitalia M, conceived and designed the study, analysed and interpreted literature data, and wrote the first drafts of the manuscripts, and approved the final version as submitted; Awang YK, contributed to the study design, analysed the data, edited references, and approved the final revision as submitted; Pratiwi R, contributed to the study design, helped with the interpretation of data, reviewed the manuscript; Utari A, contributed to the study design, analysed the data, interpreted literature data, reviewed the manuscript, and approved the final version as submitted.

Conflicts of interest

The authors declare that there is no conflict of interest.

References

Alpdemir A & Alpdemir MF (2019). Vitamin D deficiency status in Turkey: A meta-analysis. *Int J Med Biochem* 2(3):118–131.

Amrein K, Scherkl M, Hoffmann M, Sommeregger SN, Köstenberger M, Berisha AT, Martucci G, Pilz S & Malle O (2020). Vitamin D deficiency 2.0: An update on the current status worldwide. *Eur J Clin Nutr* 74:1498–1513.

Anusha K, Hettiaratchi U, Gunasekera D, Prathapan S & Liyanage G (2019). Maternal vitamin D status and its effect on vitamin d levels in early infancy in a tertiary care centre in Sri Lanka. *Int J Endocrinol* 2019:1–7.

Ariyawatkul K & Lersbuasin P (2018). Prevalence of vitamin D deficiency in cord blood of newborns and the association with maternal vitamin D status. *Eur J Pediatr* 177(10):1541–1545.

Camargo CA, Ingham T, Wickens K, Thadhani R, Silvers KM, Epton MJ, Town GI, Pattemore PK, Espinola JA, Crane J, Crane J, Dench C, Duignan M, Epton M, Fishwick D, Fitzharris P, Ingham T, Irvine V, Kelly R, Lampshire P, Lane J, Leadbitter P, MacDonald C, McCartin F, McLeod S, Nicholson A, Pattemore P, Roff K, Sawyer G, Siebers R, Town G, Wickens K, Wilson H & Withell K (2011). Cord-blood 25-hydroxyvitamin D levels and risk of respiratory infection, wheezing, and asthma. *Pediatrics* 127(1):180-187.

Choi YJ, Kim MK & Jeong SJ (2013). Vitamin D deficiency in infants aged 1 to 6 months. *Korean J Pediatr* 56(5):205-210.

Chung C, Silwal P, Kim I, Modlin RL & Jo EK (2020). Vitamin D-cathelicidin axis: At the crossroads between protective immunity and pathological inflammation during infection. *Immune Netw* 20(2):12.

Eldjerou LK, Cogle CR, Rosenau EH, Lu X, Bennett CA, Sugrue MW, Hoyne J, Lambert A, Ashley L, Sazama K, Fields G, Wingard JR & Zubair AC (2015). Vitamin D effect on umbilical cord blood characteristics: A comparison between African Americans and Caucasians. *Transfusion* 55(7):1766-1771.

Forno E, Bacharier LB, Phipatanakul W, Guilbert TW, Cabana MD, Ross K, Covar R, Gern JE, Rosser FJ, Blatter J, Durrani S, Han YY, Wisniewski SR & Celedón JC (2020). Effect of vitamin D3 supplementation on severe asthma exacerbations in children with asthma and low vitamin D levels: The VDKA randomized clinical trial. *JAMA* 324(8):752-760.

Halm BM, Lai JF, Pagano I, Cooney W, Soon RA & Franke AA (2013). Vitamin D deficiency in cord plasma from multiethnic subjects living in the tropics. *J Am Coll Nutr* 32(4):215-223.

Hassam I, Kisenge R, Aboud S & Manji K (2019). Association of vitamin D and diarrhoea in children aged less than five years at Muhimbili national hospital, Dar es Salaam: an unmatched case control study. *BMC Pediatr* 19(1):237.

Holick MF (2017). The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. *Rev Endocr Metab Disord* 18(2):153-165.

Lai SH, Liao SL, Tsai MH, Hua MC, Chiu CY, Yeh KW, Yao TC & Huang JL (2017). Low cord-serum 25-hydroxyvitamin D levels are associated with poor lung function performance and increased respiratory infection in infancy. *PLoS One* 12(3):1-13.

Long M (2017). Sun exposure. *Pediatrics* 38(9):446–447.

Meena P, Dabas A, Shah D, Malhotra RK, Madhu SV & Gupta P (2017). Sunlight exposure and Vitamin D status in breastfed infants. *Indian Pediatr* 54(2):105-111.

Mohamed WAW & Al-Shehri MA (2013). Cord blood 25-Hydroxyvitamin D levels and the risk of acute lower respiratory tract infection in early Childhood. *J Trop Pediatr* 59(1):29–35.

Oktaria V, Graham SM, Triasih R, Soenarto Y, Bines JE, Ponsonby AL, Clarke MW, Dinari R, Nirwati H & Danchin M (2020). The prevalence and determinants of vitamin D deficiency in Indonesian infants at birth and six months of age. *PLoS One* 15(10):5-12.

Oktaria V, Triasih R, Graham SM, Bines JE, Soenarto Y, Clarke MW, Lauda & Danchin M (2021). Vitamin D deficiency and severity of pneumonia in Indonesian children. *PLoS One* 16(7):5-10.

Oktaria V, Putri DAD, Ihyauddin Z, Julia M, Sulistyoningrum DC, Koon PB, Danchin M & Murni IK (2022). Vitamin D deficiency in South-East Asian children: A systematic review. *Arch Dis Child* 107:980-987.

Pratiwi R (2019). Pengaruh paparan sinar matahari terhadap kadar vitamin D pada bayi usia 7 - 12 bulan. Sp-2 *Ilmu Kesehatan Anak*. Universitas Indonesia. Jakarta.

Ruangkit C, Suwannachat S, Wantanakorn P, Sethaphanich N, Assawawiroonhakarn S & Dumrongwongsiri O (2021). Vitamin D status in full-term exclusively breastfed infants versus full-term breastfed infants receiving vitamin D supplementation in Thailand: a randomized controlled trial. *BMC Pediatr* 21(1):378.

Rueter K, Jones AP, Siafarikas A, Lim EM, Prescott SL & Palmer DJ (2020). In "high-risk" infants with sufficient vitamin D status at birth, infant vitamin D supplementation had no effect on allergy outcomes: A randomized controlled trial. *Nutrients* 12(6):7-9.

Searing DA & Leung DYM (2010). Vitamin D in atopic dermatitis, asthma and allergic diseases. *Immunol Allergy Clin North Am* 30(3):397–409.

Streym SV, Højskov CS, Møller UK, Heickendorff L, Vestergaard P, Mosekilde L & Rejnmark L (2016). Vitamin D content in human breast milk: A 9-mo follow-up study. *Am J Clin Nutr* 103(1):107-114.

Streym SV, Moller UK, Rejnmark L, Heickendorff L, Mosekilde L & Vestergaard P (2013). Maternal and infant vitamin D status during the first 9 months of infant life-a cohort study. *Eur J Clin Nutr* 67(10):1022-1028.

Wang DY (2011). Genetic predisposition for atopy and allergic rhinitis in the Singapore Chinese population. *Asia Pac Allergy* 1(3):152–156.

Wang H & Chow SC (2007). Sample size calculation for comparing proportions. Wiley Encyclopedia of Clinical Trials.

WHO & UNICEF (2021). Indicators for assessing infant and young child feeding practices: Fefinitions and measurement methods. Geneva. Licence: CC BY- NC-SA 3.0 IGO