Are Infants Exclusively Breastfed up to 6 Months of Age at Risk of Anemia?

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Objective: *To compare the incidence of anemia between infants who received exclusive breast feeding (EBF) up to the age of 6 months and those who did not.*

Material and Method: *A cross sectional survey was conducted to examine the physical growth, incidence of anemia, mean hematocrit (Hct) level and other red cell indices among 6-month-old infants visiting a well-child clinic at QSNICH and Ramathibodi Hospital.*

Results: *63 infants were included in the present study: 24 (38%) EBF group; and 39 (62%) non-EBF group. Mean Hct of EBF group was 34.5 ± 1.7 and Non-EBF group was 35.1 ± 2.3% respectively. The prevalence of anemia in the EBF group was 4.2%, non-EBF group was 12.8%. Even though the findings were not statistically significant, the authors found that the red blood cell indices in an anemic infant in the EBF group were not caused by iron deficiency, while the 4 of 5 anemic infants in the Non-EBF group were related to iron deficiency anemia (80%). Other growth parameters were compared between the two groups.*

Conclusion: *The present study did not show statistical difference regarding the different hematocrit and other red blood cell indices including other fundamental background but the prevalence of anemia appeared to be higher among Non-EBF compared to EBF up to 6 months. The cause of anemia was not related to iron deficiency anemia in the EBF group compared to those higher and related to iron deficiency anemia in the Non-EBF group.*

Suggestion*: EBF up to 6 months should be advocated given its substantial health benefit and does not increase the risk of anemia. Nevertheless, it is essential that mothers receive adequate nutritional supplement including iron during pregnancy and lactation period.*

Keywords*: Exclusive breastfeeding (EBF), Anemia, Infant*

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Recently, the World Health Organization has recommended the extended duration of exclusive breast feeding for infants up to 6 months of age[1] owing to the existing evidence supporting the protective effect of exclusive breastfeeding (EBF) on gastrointestinal and respiratory illness[2,3]. In addition, EBF appears to reduce the risk of allergy as well as enhance infant's cognitive development. However, concerns were raised about potential nutritional deficiency such as iron deficiency anemia among infants with EBF due to lack of supplementary diet.

Existing evidence supporting the lack of iron deficiency anemia among infants receiving EBF are as follows. Duncan et al conducted a survey among 30 infants with 6 months duration of EBF. The results indicated that 12% and 13% of these infants had low MCV and serum ferritin, respectively. However, none of them were anemic[3]. Lonnerdal and Hernall evaluated 10 infants receiving EBF compared with those who received infant formula (with 4-7 mg/L iron) with non-iron fortified supplementary diet before 6 months of age. There was no significant difference between the levels of hemoglobin, serum iron, MCV and serum transferrin receptors between the two groups at 6 weeks and 6 months of age[4]. In addition, a study conducted by Siimes et al demonstrated that no infants receiving EBF was anemic or had any signs of iron deficiency at the age of 6 months[5].

In contrast, a study conducted in Argentina found that up to 44% of infants receiving EBF up to 6 months of age were anemic, compared to only 14.3%

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among those who received infant formula at the age of 6 months of life. At 9 months of age, anemia was detected in 22.8% among those with EBF and 7.1% among the non-EBF group[6].

In 1990, Pizarro F et al conducted a survey among 3 different feeding groups at the age of 9 months: those who received infant formula, breast feeding and iron-fortified infant formula. Iron deficiency anemia was detected in 37.5%, 26.5% and 8% among those receiving infant formula, breast feeding and iron-fortified infant formula, respectively. However, all infants had received supplementary diet since the age of 3 months[7]. Maternal iron status may have a certain effect on the incidence of anemia of their infant. However, the relationship between these variables has not been adequately addressed. According to existing evidence, infants receiving supplementary diet before the age of 6 months may be at a higher risk of iron deficiency anemia. Therefore, the objective of the present study was to examine the incidence of having anemia between

Table 1. Maternal socio-demographic characteristics by feeding patterns

Variables	EBF group	Non-EBF group	p-value
Mean age (year)	29.11 ± 6.69	28.18 ± 7.08	0.16
Mode of family income	10,000-20,000 (50%)	5,000-15,000 (55.13%)	0.882
Percentage of unemployment	70.8%	30.8%	0.02
Attainment of high school education	33.3%	38.5%	0.326
Mean number of children (SD)	1.8 (0.7)	1.6 (0.7)	0.436
Proportion receive vitamin supplement	100%	97.4%	0.619
Percentage of normal labor	58.3%	59.0%	0.387
Percentage of full time mother	87.5%	66.7%	0.168

EBF: exclusive breast feeding

Table 2. Infant characteristics by feeding pattern

Characteristics	EBF	Non-EBF	p-value
Male: female ratio	10: 14	20: 19	0.315
Birth weight (gram)	3,247.29 ± 243.15	3,120.95 ± 394.52	0.164
Weight at 6 months of age (gram)	7,725.0 ± 783.67	7,761.54 ± 982.11	0.878
Length at birth (cm)	50.84 ± 1.71	50.45 ± 1.83	0.437
Length at 6 months of age (cm)	65.45 ± 3.49	65.14 ± 2.78	0.703
Head circumference at birth (cm)	33.66 ± 1.143	33.38 ± 1.38	0.452
Head circumference 6 months of age (cm)	42.39 ± 1.77	42.42 ± 1.85	0.940

Table 3. Infants' red blood cell indices by feeding pattern

Indices	EBF	Non-EBF	p-value	95% CI
Hb (g/dl)	11.49 ± 0.58	11.52 ± 0.81	0.862	-0.348, 0.414
Hct (%)	34.49 ± 1.72	35.09 ± 2.31	0.270	-0.484, 1.701
MCV (fL)	72.98 ± 5.42	73.39 ± 5.99	0.785	-2.591, 3.415
MCH (pg)	24.26 ± 1.85	24.13 ± 2.12	0.801	-1.183, 0.918
MCHC (g/dl)	33.25 ± 1.07	32.86 ± 0.97	0.143	-0.910, 0.134
RDW (%)	15.02 ± 1.57	14.94 ± 2.04	0.869	-1.053, 0.892
Reticulocyte count (%)	0.75 ± 0.36	0.88 ± 0.35	0.172	-0.58, 0.317

Hb: hemoglobin, Hct: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width

infants receiving EBF up to the age of 6 months and those not receiving EBF.

Material and Method

Data were collected through face-to-face individual interviews with caregivers of 6-month-old infants attending the well-baby clinic at Queen Sirikit National Institute of Child Health (Children's Hospital) and Ramathibodi Hospital, Bangkok, Thailand from October 2005 to September 2006. Blood samples from infants were obtained for hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and reticulocyte count, and peripheral blood smear. Eligible criteria for infant participants included: 1) Term infants with birth weight between 2,500 and 4,000 grams; 2) No maternal illness without risk factors of anemia nor pregnancy complication *e.g.*, anemia, blood loss or diabetes; 3) No underlying illness *e.g.*, heart disease, anemia, major congenital anomalies, and other chronic illness; 4) No current or recent illness during the past 2-week period prior to blood withdrawal; 5) Having the ability and willingness to provide written informed consent. Sample size calculation was based on the data from a study conducted in Argentina which indicated that percentage of anemia among infants receiving EBF and those receiving infant formula were 44% and 14.3%, respectively[6]. The formula used to calculate the sample size is shown as follows:

$$n_0 = \frac{[Z_{\alpha/2}\sqrt{pq\,(\lambda + 1)/\lambda} + Z_{1-\beta}\sqrt{p_0q_0 + p_1q_1/\lambda}]^2}{[p_1 - p_0]^2}$$

where $p = (p_0 + \lambda\, p_1)/(1 + \lambda)$; $q = 1 - p$; and $Z_{\alpha/2} = 1.96$, $Z_\beta = 0.84$

p_0 = proportion of anemia among infants receiving EBF until 6 months = 0.44

p_1 = proportion of anemia among infants not receiving EBF = 0.14

$q_0 = 1 - p_0 = 0.56$

$q_1 = 1 - p_1 = 0.86$

$p = (0.44 + 0.14)/2 = 0.29$

$q = 1\text{-}0.29 = 0.71$

n_0 = number of infants receiving EBF until 6 months

n_1 = number of infants not receiving EBF until 6 months

$\lambda = n_1/n_0$, which is set at 1

$n_0 = \{1.96\sqrt{[(0.20)(2)]} + 0.84\sqrt{[(0.25)+(0.12)]}\}^2 / \{0.3\}^2 = 33.64$

Therefore, sample size for each group was estimated as 35 infants/group. Group 1 consisted of infants receiving EBF and group 2 consisted of infants receiving mixed feeding (both breast feeding and formula feeding) and only formula feeding. Data obtained from individual interview consisted of socio-demographic data *e.g.*, maternal age, household income, number of siblings, gestational age, mode of delivery, maternal health, family history of anemia, history of iron and vitamin supplement during gestation, infant feeding practices. Indicators of physical growth, such as body weight and length; head circumference at birth and at 6 months, were also collected. Descriptive analysis was used for basic demographic data. Fischer's exact test and Chi-square tests were used to compare variables between the two groups when appropriate with the significant level at 0.05.

Results

During the 12 month period of recruitment, 24 and 39 infants belonged to EBF and non-EBF groups were enrolled (n = 63). The mean hematocrit of all infant participants was 34.9% (range 30.1-40.2%). Mean hematocrit of EBF group was 34.5 $\pm$ 1.7 and Non-EBF group was 35.1 $\pm$ 2.3% which were not statistically significantly different. In addition, other red cell indices (hemoglobin, MCV, MCH, MCHC, RDW and reticulocyte count) were comparable between the two groups. Anemia (hematocrit less than 33%) was detected in 6 infants, 1 (4.2%) among EBF group, 5 (12.8%) among non-EBF group ($p > 0.05$). Although the prevalence of anemia were approximately three times higher among the non-EBF group, the result was not statistically significant.

Regarding the cause of anemia, the infants in the EBF group (one case) had Hematocrit level less than 33% but the MCV, RDW were normal and also the peripheral blood smear was normochromic and normocytic. No evidence suggesting that it was a result of iron deficiency or hemolysis. The anemic infants in the non-EBF group (4 out of 5 cases) had low Hemoglobin, Hematocrit, MCV and Reticulocyte count. Their peripheral blood smear showed hypochromic, microcytic, without evidence of hemolysis. One case of an anemic infant in this group had the same blood picture as an anemic case in EBF group. These findings indicated that four out of five cases (80%) in non-EBF were iron deficiency anemia.

The physical growth parameters including weight, length and head circumference at the age of birth and 6 month-old were relatively comparable between the two groups. Baseline maternal socio-demographic variables were rather comparable except

for the higher proportion of stay-at-home mothers who were not employed among the EBF group than non-EBF group (70.8% vs. 30.8%).

Discussion

The present study set out to determine the prevalence of iron deficiency anemia among 6 month-old infants receiving EBF and those who were not. In addition, the authors also compared maternal socio-demographic status between these two groups. Our results indicated that although there was a significantly higher proportion of maternal unemployment rate among EBF infants, other socio-demographic variables including household income were rather comparable between the 2 groups. The authors speculated as these mothers were not employed, they had a higher chance of successfully breast feed their infants.

Similar to existing reports by Eregie and Duncan, the present finding added the existing evidence that exclusive breastfeeding does not appear to increase the risk of iron deficiency anemia when comparing formula feeding among 6-month-old infants. In contrast, the prevalence of anemia appeared to be higher, although not statistically significant, among formula-fed infants (12.8%) compared to exclusively breastfed infants (4.2%). In addition, the result of investigation revealed that anemia detected in an exclusively breastfed infant was not caused by iron deficiency whereas 80% of anemia among non-EBF infants was as attributable to iron deficiency. Further, none of the red blood cell indices and physical growth parameters significantly differed between the two groups. The present findings corroborate with existing reports by Lonnerdal and Siimes indicating that exclusive breastfeeding up to 6 months of age posed no increase in risk of having iron deficiency anemia[5,8]. In addition, a study by Pisacane indicated that infants who received EBF more than 7 months were able to maintain normal iron status by the age of 12 and 24 months[9].

Of important note, the present results showed that red blood cell indices appeared to be lower than the reference value reported in a medical textbook[10,11]. It is possible that the standard value of red blood cell indices of Thai infants may be lower than those reported from Western countries. However, the authors do not have a large enough sample size or representative sample to establish the reference value for the red blood cell indices of Thai infants.

Although the current study suggests that EBF up to the age of 6 months posed no increase in the risk of iron deficiency anemia, it is essential that mothers receive adequate nutritional supplement including iron during the entire nursing period. In addition, mothers should be informed that supplementation with other types of food during the first six months of life can interfere with iron absorption from breast milk. Therefore, maintaining exclusive breast feeding status is essential to ensure the normal iron status of, and adequate milk supply for, their infants.

Potential conflicts of interest

None.

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ทารกที่ได้รับนมแม่อย่างเดียว ถึงอายุ 6 เดือน เสี่ยงต่อการเกิดภาวะเลือดจางหรือไม่

ศิราภรณ์ สวัสดิวร, สุวรรณา แท้วิริยะกุล

วัตถุประสงค์ *: เพื่อศึกษาอุบัติการณ์ภาวะโลหิตจาง เปรียบเทียบระหว่างทารกที่ได้รับนมแม่อย่างเดียว ถึงอายุ 6 เดือน (EBF) กับกลุ่มที่ไม่รับนมแม่อย่างเดียวถึงอายุ 6 เดือน (non-EBF)*

วัสดุและวิธีการ*: การศึกษาแบบตัดขวาง โดยตรวจสภาวะการเจริญเติบโต, อุบัติการณ์โลหิตจาง, สภาวะความเข้มข้นของเม็ดเลือดแดง (Hematocrit, Hct) และค่าชี้วัดเม็ดเลือดแดงอื่นๆ ของทารกอายุ 6 เดือนที่มารับบริการในคลินิกสุขภาพเด็กดีในสถาบันสุขภาพเด็กแห่งชาติมหาราชินี และที่โรงพยาบาลรามาธิบดี*

ผลการศึกษา*: ทารกจำนวน 63 ราย แบ่งเป็นกลุ่ม EBF จำนวน 24 ราย (ร้อยละ 38) และกลุ่ม Non-EBF จำนวน 39 ราย (ร้อยละ 62) กลุ่ม EBF และ Non-EBF มีค่า Hematocrit เฉลี่ยเท่ากับร้อยละ 34.5$\pm$1.7 g/dl และ 35.1$\pm$2.3 g/dl ตามลำดับ กลุ่ม EBF มีภาวะโลหิตจาง 1 คน คิดเป็นร้อยละ 4.2 กลุ่ม Non-EBF พบภาวะโลหิตจาง 5 คน คิดเป็นร้อยละ 12.8 ไม่พบความแตกต่างทางสถิติในค่าตัวชี้วัดดังกล่าวของทั้งสองกลุ่ม มีข้อสังเกตพบว่าทารกมีภาวะโลหิตจางในกลุ่ม EBF ไม่พบหลักฐานว่าเป็นจากการขาดธาตุเหล็ก ในขณะที่พบหลักฐานภาวะโลหิตจางจากการขาดธาตุเหล็กในกลุ่ม Non EBF 4 ใน 5 ราย คิดเป็นภาวะขาดธาตุเหล็กร้อยละ 80 ทารกทั้งสองกลุ่มไม่มีความแตกต่างกันทางสถิติในด้านการเจริญเติบโต*

สรุป*: การศึกษานี้ไม่พบความแตกต่างที่มีนัยสำคัญทางสถิติทั้งในด้านความแตกต่างของค่าความเข้มข้นของเม็ดเลือดแดง และค่าชี้วัดเม็ดเลือดแดงอื่นๆ รวมทั้งข้อมูลพื้นฐาน แต่มีข้อมูลให้เห็นว่าทารกที่ได้รับนมแม่อย่างเดียว 6 เดือน มีภาวะโลหิตจางน้อยกว่า กลุ่มที่ไม่ได้รับ และภาวะโลหิตจางที่พบก็ไม่มีข้อบ่งชี้ว่าเป็นจากการขาดธาตุเหล็ก ในขณะที่กลุ่ม ไม่ได้รับมีตัวชี้วัดว่าเป็นผลจากการขาดธาตุเหล็กถึงร้อยละ 80*

ข้อเสนอแนะ*: ควรส่งเสริมให้ทารกได้รับนมแม่อย่างเดียว 6 เดือน จากประโยชน์ที่จะมีผลดีต่อสุขภาพแม่ลูก และไม่น่ามีผลเพิ่มโอกาสโลหิตจาง อย่างไรก็ตามต้องให้ความสำคัญกับการที่แม่ได้รับอาหาร วิตามิน เกลือแร่ที่เพียงพอระหว่างตั้งครรภ์ และในระหว่างให้นมบุตร*