

The potential of a simple egg to improve maternal and child nutrition

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Abstract

Evidence is mounting about the benefits of eggs for child nutrition and potential benefits for women during pregnancy and birth outcomes. Maternal consumption of eggs during lactation may also enhance the breast-milk composition of certain nutrients, thus contributing to the nutrition and potentially also to the development of breastfed children. Relative to single nutrient supplements, eggs deliver nutrients and other hormone or immune factors in compounds that may be more readily absorbed and metabolized. In addition to macronutrients, eggs contain a number of micronutrients, such as choline, that are known to have brain health promoting effects. Among children less than 2 years of age, consumption nearly universally increases with age. Large regional differences exist; the prevalence of egg consumption among African children is less than half that of most other world regions and threefold less than in Latin America and the Caribbean. Among women of reproductive age, egg consumption is strongly related to socio-economic status in a dose-response fashion with women in the lowest wealth quintile eating the fewest eggs and those in the highest wealth quintile eating the most. Cultural factors likely play a role in around consumption of eggs during pregnancy, lactation, and early childhood, though most reports are anecdotal in nature and few high-quality data exist. Well-informed social marketing and behaviour change communication strategies have led to large increases in egg consumption among young children. Economic barriers that limit access are likely to be far more important than cultural ones in explaining low consumption.

KEYWORDS

brain development, breast milk, child nutrition, eggs, maternal nutrition

1 | INTRODUCTION

Chickens eggs are ubiquitous globally and well known to be highly nutritious, yet are generally not widely consumed among children and women of reproductive age in low- and middle-income countries (Iannotti, Lutter, Bunn, & Stewart, 2014; Lutter, Iannotti, & Stewart,

2016). Yet evidence is mounting about their benefits to child nutrition and potential benefits for women during pregnancy and birth outcomes. The Lulun Project, a randomized controlled trial conducted among young undernourished children in the Ecuadorian Andes, showed dramatic effects on growth and stunting reduction after consuming eggs for just 6 months (Iannotti, Lutter, Stewart, et al., 2017). It also showed significant effects on biomarkers of choline and docosahexaenoic acid (DHA) status, two nutrients associated with cognitive development, raising the question whether eggs early in the complementary feeding period might also

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contribute to child development (Iannotti, Lutter, Stewart, et al., 2017).

Building on our previous review (Iannotti et al., 2014), here, we highlight the contribution of eggs to maternal and child nutritional requirements, how maternal consumption of eggs may influence breast-milk composition, how specific of key nutrients in eggs likely contribute to brain development, and the role of cultural beliefs and egg taboos around egg consumption. We also provide recent national and regional data on egg consumption among young children in low- and middle-income countries.

2 | RESULTS

2.1 | Contribution of eggs to the nutrient requirements of young children and pregnant and lactating women

Eggs are holistically designed for reproduction and nutritive support for the chicken embryo from conception to the time it hatches. As such, they provide the sole source of immune protection and nutrients until the chick can survive independently in the environment. The distinctive parts of the egg—the yellow yolk, white, and shell—differ in both composition and biological function. Although the yolk's composition is primarily nutritive, the purpose of the white serves mainly as a defence mechanism against pathogens. The shell is a semipermeable membrane to allow for air and moisture to pass through its pores, and has as a thin outermost coating that helps keep out bacteria and dust.

One egg has, on average, only 75 calories but 7 g of high-quality protein, 5 g of fat, and 1.6 g of saturated fat, along with vitamins, minerals, and carotenoids. The egg is also high in disease-fighting dietary bioactive compounds such as lutein and zeaxanthin, which may reduce the risk of age-related macular degeneration, the leading cause of blindness in older adults (Wallace, 2018). Animal models show lutein and zeaxanthin also help to protect against oxidative stress (Bian et al., 2012).

Eggs are particularly high in choline, an important precursor of phospholipids, which are needed for cell division, growth, and membrane signalling (Caudill, 2010; Zeisel & Niculescu, 2006). Inadequate intake during pregnancy has been associated with neural tube defects (Shaw, Carmichael, Yang, Selvin, & Schaffer, 2004), changes in brain structure and function in the offspring (Zeisel & Niculescu, 2006) and adverse pregnancy outcomes (Vollset et al., 2000). Choline may influence gene expression, including epigenetic effects, during pregnancy because of its role as a methyl donor (Jiang et al., 2012). Choline supplementation during late pregnancy resulted in significant changes in expression of genes regulating placental vascularization and angiogenesis (Jiang et al., 2012). This suggests that choline may affect placental development and remodelling, required for placental perfusion and nutrient transfer, particularly with respect to Docosahexaenoic acid (DHA). Brain development and memory may be enhanced by the choline content of eggs (see later section).

During pregnancy and early childhood, cells of the fetus and child grow in size and number at a rapid rate, requiring a steady and

Key messages

- Eggs provide an exceptional protein source as well as fatty acids and a large range of vitamins, minerals, and bioactive compounds that could potentially improve birth outcomes, child nutrition, and brain development.
- Relative to single nutrient supplements, eggs deliver nutrients and other hormone or immune factors in compounds that may be more readily absorbed and metabolized.
- Egg consumption is low among women of reproductive age and young children with the lowest intakes in the African region, India, and among children 6 to 8 months of age in all regions.
- Cultural factors play a role in many nutrition practices, including around consumption of eggs during pregnancy and early childhood, though most reports are anecdotal.
- Carefully conducted social marketing and behaviour change communication strategies have led to large increases in egg consumption among young children.

increasing source of nutrients. The high quality of essential macronutrients provided by eggs can contribute to optimizing these processes. Protein quality plays an important role during this period. An ideal food during this period is one with a high digestible indispensable amino acid score (FAO, 2013) with eggs and milk having the highest scores. Although protein deposition in maternal and fetal tissues increases throughout pregnancy, most occurs in the third trimester. A single estimated average requirement for protein covers all pregnancy, which does not take into consideration changing needs as a pregnancy progresses. Protein requirements may be 14% to 18% greater than the current recommendation according to recent research (Elango & Ball, 2016). Eggs are also an important source of essential fatty acids. DHA, in particular, is critical for early brain growth and visual acuity (Hoffman et al., 2004; Riediger, Othman, Suh, et al., 2009). Limited evidence suggests that essential fatty acids during pregnancy might have benefits for birthweight and length and gestational age (Huffman, Harika, Eilander, & Osendarp, 2011). Early in pregnancy, maternal cholesterol plays an important role in placental hormone biosynthesis, implementation, and vascularization; low levels may result preterm birth and other adverse birth outcomes (Edison et al., 2007).

For a number of key nutrients, eggs provide a large proportion of the Recommended Dietary Allowance (RDA) or adequate intake (AI) for young children as well as pregnant and lactating women (Table 1). For a healthy infant between 7 and 12 months of age, one 50-g egg provides 57% of the RDA for protein. It provides 88% and 98% of the AI for vitamin B₁₂ and choline, respectively. It provides between 25% and 50% of the AI for pantothenic acid, vitamin B₆, folate, phosphorus, and selenium and slightly over 20% of the requirement for zinc. For a breastfed infant consuming an average

TABLE 1 Nutrient content of one large egg and proportion of adequate intake (AI) or recommended dietary allowance (RDA) level for healthy breastfed infants aged 7–12 months and two large eggs for pregnant and lactating women

Nutrient	Unit of measure	Large egg (50 g)	% AI/RDA for healthy infant 7–12 months provided by 1 large egg	% AI/RDA during pregnancy provided by 2 large eggs	% AI/RDA during lactation provided by 2 large eggs
Energy	kcal	72	–	–	–
Protein	g	6.28	57.3	17.7	17.7
Lipids (total)	g	4.75	–	–	–
Linoleic acid (18:2n-6)	g	0.77	16.7	11.8	11.8
α -Linolenic acid (18:3n-3)	g	0.02	4.0	2.9	3.1
DHA (22:6n-3)	g	0.03	–	–	–
Carbohydrates	g	0.36			
Vitamins					
Vitamin A, RAE	ug	80.0	16.0	20.8	12.3
Thiamin (B ₁)	mg	0.02	6.7	2.8	2.8
Riboflavin (B ₂)	mg	0.23	57	32.6	28.5
Niacin (B ₃)	mg	0.04	1.0	0.4	0.3
Pantothenic acid (B ₅)	mg	0.77	42.8	25.7	22.0
Vitamin B ₆	mg	0.09	28.3	8.9	8.5
Vitamin B ₁₂	ug	0.44	88	33.8	31.4
Folate DFE	ug	24	30	8.0	9.6
Choline	mg	146.9	97.9	65.3	53.4
Vitamin C (ascorbic acid)	mg	0	0	0	0
Vitamin D (D ₂ + D ₃)	ug	1.0	10.0	13.3	13.3
Vitamin E (a-tocopherol)	mg	0.52	10.4	6.9	5.5
Vitamin K	ug	0.2	0.8	0	0
Minerals					
Calcium	mg	28	10.8	5.6	5.6
Copper	mg	0.04	18.2	8.0	6.2
Iodine	ug	0	0	0	0
Iron	mg	0.88	8.0	6.5	19.6
Magnesium	mg	0.6	8.0	3.4	3.9
Manganese	mg	0.01	2.3	1.4	1.1
Phosphorus	mg	99.0	36	28.3	28.3
Potassium	mg	69.0	9.9	2.9	2.7
Selenium	ug	15.4	77	51.3	44.0
Sodium	mg	71.0	–	–	–
Zinc	mg	0.64	21.3	11.6	10.7

Note. DFE, dietary folate equivalents; DHA, docosahexaenoic acid; RAE, retinol activity equivalents. For infants, calculations used the RDA for protein, iron, and vitamin D and the AI for all other nutrients. For pregnant and lactating women, calculations used the AI for vitamin K, choline, pantothenic acid, manganese, and potassium and the RDA for all other nutrients. AIs/RDAs from the Food and Nutrition Board, Institute of Medicine, National Academies. For thiamin, riboflavin, niacin, vitamin B₆, folate, vitamin B₁₂, pantothenic acid, and choline (1998); for vitamin C, vitamin E, and selenium (2000); for vitamin A, vitamin K, copper, iodine, iron, manganese, and zinc (2001); potassium and sodium (2005); and calcium and vitamin D (2011). (Institute of Medicine, Food and Nutrition Board, & National Academy of Sciences). Institute of Medicine, Food and Nutrition Board, & National Academy of Sciences. Dietary Reference Intakes (DRIs): Estimated Average Requirements. <http://www.nationalacademies.org/hmd/~media/Files/Activity%20Files/Nutrition/DRI-Tables/5Summary%20TableTables%2014.pdf?la=en>, accessed March 15, 2018.

amount of breast milk (World Health Organization [WHO], 1998), one 50-g egg provides 29% of energy needs. For pregnant women, two 50-g eggs provide 18% of the RDA for protein. They provide between 20% and 35% of the AI/RDA for vitamin A, riboflavin, pantothenic acid, vitamin B₁₂, and phosphorus. They also provide more than 50% of AI/RDA for choline and selenium. For lactating women, a same amount of eggs provide between 20% and 35% of requirements for riboflavin, pantothenic acid, vitamin B₁₂, iron, and phosphorus. They provide 53% and 44% for choline and selenium, respectively.

2.2 | Eggs and nutrient composition of breast milk

Maternal consumption of eggs during lactation may also enhance the breast-milk composition of choline and other water-soluble vitamins, thus contributing to child nutrition and potentially the optimal development of breastfed children. A mother's intake of water soluble vitamins largely affects the concentration of nutrients in breast milk. To a lesser extent, breast-milk concentration is influenced by intake and stores of fat-soluble vitamins (WHO, 1998). Micronutrients have been classified into two groups, according to the effect of maternal intake

and the status of the micronutrient content of breast milk (Allen, 2012). In Group 1 are those affected by maternal status including thiamin, riboflavin, vitamin C, vitamin D, vitamin B₆, vitamin B₁₂, choline, vitamin A, iodine, and selenium. In Group 2 are those not affected by maternal status including folate, calcium, iron, copper, and zinc. During lactation, low maternal intake or stores of micronutrients in Group 1 reduces the amount in breast milk, which may negatively affect a child's growth and possibly development. As noted above, breast milk is particularly rich in choline, the concentration of which doubles after birth (Homes, Snodgrass, & Iles, 2000). Adequate intake of Group 1 micronutrients is necessary to ensure breast-milk adequacy and eggs are high in several of these, including choline, riboflavin, and vitamin B₁₂.

Fatty acids in breast milk are also extremely sensitive to maternal consumption and body composition, with implications for infants' neurological development (Innis, 2014). The transfer of n-6 (omega-6) and n-3 (omega-3) fatty acids from the maternal diet into breast milk occurs with little interconversion of 18:2n-6 to 20:4n-6 or 18:3n-3 to DHA. There is also little evidence of regulation by the mammary gland to maintain individual fatty acids constant with varying maternal fatty acid nutrition. A recent study among Chinese women showed that supplementation of DHA during pregnancy increases the concentration of polyunsaturated fatty acids in breast milk (Deng et al., 2016).

2.3 | Eggs and brain development and function

Finding from the Lulun Project in Ecuador suggests consumption of eggs during early childhood could contribute to healthy brain development and function (Iannotti, Lutter, Waters, et al., 2017). In the Lulun Project, children in the egg intervention group had significantly higher concentrations of biomarkers associated with improved child development and important physiological processes in the brain. Choline concentrations were increased by an effect size of 0.35 and DHA by 0.43. Although child development outcomes were not assessed, qualitative research findings pointed to increases in child activity levels and social interactions with caregivers and others (Waters et al., 2018). However, inasmuch as these findings were reported by mothers and caregivers in the intervention group, the study team acknowledges the potential for performance bias.

The nutrient composition, and likely more importantly the nutrient matrix of the egg, has potential to impact brain growth and development. Relative to single nutrient supplements, eggs may deliver nutrients and other hormone or immune factors in compounds that are more readily absorbed and metabolized. The concept of food synergies may be applied here to understand how egg nutrients and other factors act in concert to contribute to growth and development (Jacobs & Tapsell, 2007). The protein content of eggs, held up as the standard for amino acid composition for decades, may contribute to meeting protein needs of mothers and children but eggs also package minerals such as iron or zinc in bioavailable forms.

Here, we highlight particular nutrients found in eggs and their role in brain development as evidenced in the literature, though again in recognition that matrices of multiple assembled nutrients together likely impact outcomes. DHA, although not as highly concentrated in eggs compared with fish foods, was significantly increased in the Lulun Project. This essential fatty acid contributes to neurogenesis,

neurotransmission, myelination, and synaptic plasticity, among other processes (Weiser, Butt, & Mohajeri, 2016). Evidence shows the importance of DHA through the lifespan for cognition and visual acuity (Uauy & Dangour, 2006). Another long-chain fatty acid, arachidonic acid (ARA), is derived from linoleic acid found more highly concentrated in eggs. ARA contributes to signalling and hippocampal plasticity. Its role in potentiation may arise from the production of docosahexaenoic (adrenic) acid from ARA (Hadley, Ryan, Forsyth, Gautier, & Salem, 2016).

In addition to macronutrients, several micronutrients are known to have brain health promoting effects (Goyal, Iannotti, & Raichle, 2018). Choline is an important precursor for the neurotransmitter, acetylcholine, and sphingomyelin, a lipid molecule that surrounds neuronal axons for insulation and signal transduction purposes. Animal models have demonstrated choline's role in hippocampal development and function, whereas in humans, studies indicate its importance for long-term memory and cognition (Zeisel, 2006). A recent trial in the United States showed that maternal choline supplementation in the third trimester improved infant information processing speed (Caudill, Strupp, Muscalu, Nevins, & Canfield, 2017). Vitamins A (as retinol) and B₁₂, both present in eggs and with established functions in brain development, were not increased in the Lulun Project. Selenium was not assessed in Lulun, but in view of its high concentration in eggs providing over 75% of daily requirements for infants 7–12 months and role in brain development and thyroid metabolism, more studies could examine its effects. Iron and zinc, although provided in small quantities in eggs, could contribute to brain development. Iron participates in myelination synthesis, neurotransmitter metabolism, and neurotransmitter metabolism (Beard & Connor, 2003). Zinc activity in the brain is known to be primarily at the synaptic cleft, in glutamatergic processes, but also in critical roles in DNA and RNA synthesis and transcription and enzyme activity, among others (Levenson & Morris, 2011). Deficiencies in both iron and zinc during childhood are known to compromise child development.

Eggs and other animal source foods (ASF) have long been part of the hominid diet, beginning approximately during the juncture in evolution when brain size increased compared with other primates (Eaton & Iannotti, 2017). Sea bird eggs in particular are considered part of the shore-based paradigm that explains rapid brain growth arising from lacustrine and marine foods during the Palaeolithic period (Cunnane & Crawford, 2014). With the advent of agriculture and rapid industrialization in the past two centuries, the proportion of ASF in the diet relative to cereals and processed foods has decreased especially in low- and middle-income countries. The evolutionary history of eggs and brain growth may contribute to the rationale for ensuring eggs in the diets of mothers and children. Although we have focused on maternal and young child nutrition, eggs also have the potential to improve brain development and functioning throughout the lifecycle (Wallace, 2018).

2.4 | Egg consumption among young children and women of reproductive age

Egg consumption in the previous 24 hr among young children is highly variable, though two broad patterns are discernable (Figure 1; Appendix S1). Consumption nearly universally increases with age

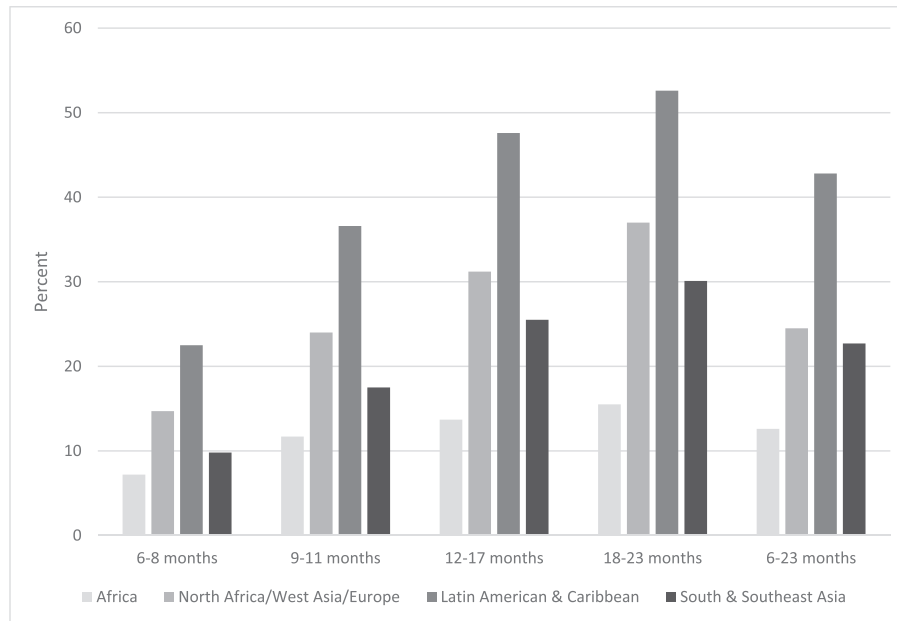


FIGURE 1 Regional prevalence (%) of egg consumption in the previous 24 hr among children less than 2 years of age, based on nationally representative surveys conducted 2006–2017 and weighted for age-specific population size of countries represented. Consumption data calculated from ICF International, the DHS Program, Demographic and Health Surveys (DHS StatComplier, accessed March 12, 2018). Population estimates to construct weighted regional averages from United Nations, World Population Prospects: The 2017 Revision

across all regions. Large regional differences are also apparent; the prevalence of egg consumption among African breastfed children is less than half that of most other world regions and threefold less than the region of Latin America and the Caribbean.

Few data are available on egg consumption among women of reproductive age as questions about food intake in the preceding 24 hr were only asked in a subset of Demographic and Health Surveys conducted between 2007 and 2010 for women who had given birth in the last 3 years and were dropped in subsequent surveys.

Among this group, egg consumption was strongly related to socio-economic status in a dose–response fashion with women in the lowest wealth quintile eating the fewest eggs and those in the highest wealth quintile eating the most (United States Agency for International Development, Dec 2014; Figure 2). However, the differences in consumption by wealth quintile were also quite variable; for example, although the difference between the lowest and highest quintile in Ghana ranged from 13.8% to 31.8%, in Tanzania, it only ranged from 3.1% to 9.4%.

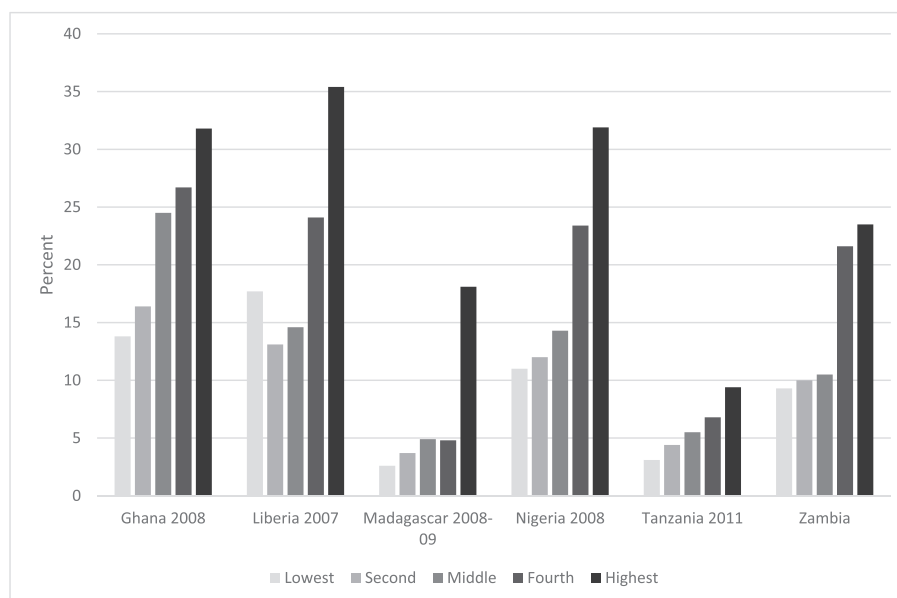


FIGURE 2 Prevalence (%) of egg consumption in previous 24 hr among women age 15–49 years who gave birth in the last 3 years by household wealth quintile, based on nationally representative surveys conducted 2007–2010. United States Agency for International Development (Dec 2014) nutrition status of women and children. A 2014 update on nutritional status by socio-economic and water, sanitation, and hygiene indicators collected in Demographic and Health Surveys. Rockville, Maryland USA. ICF International

2.5 | Cultural and belief barriers around egg consumption

Cultural factors play a role in many nutrition practices, including taboos or beliefs around consumption of eggs during pregnancy, lactation, and early childhood, though most reports are anecdotal in nature and few quantitative or qualitative studies on the subject exist. In Bangladesh, the 2007 Demographic and Health Survey showed that 75% of children 2 to 3 years had consumed eggs, fish, or poultry the preceding day whereas only 10% of infants 6 to 7 months had consumed these foods, showing that beliefs about what and when young children should receive ASF, including eggs, are extremely important (Jimerson, 2017). Among pregnant women in Nepal, religion has been cited reason for not eating eggs (Christian et al., 2006).

In rural Zambia, Dumas et al., (this supplement) report that over 90% of women agreed eggs were good for infants and young children, 82% agreed they were good for pregnant women, and 90% agreed they were good for lactating women. Taboos restricting egg consumption by certain individuals, most commonly pregnant women, were only voiced by only 8% of women.

It is likely that cultural barriers and egg taboos may be overcome with well-informed and carefully conducted social marketing and behaviour change communication strategies (Pelto, Armar-Klimesu, Siekmann, & Schofield, 2013) and evidence to support this is available for young children. In a recent large-scale intervention in Bangladesh that heavily promoted egg consumption for young children 6 to 24 months, consumption among children in the intensive intervention group increased from 18% to 48% compared with only 19% to 31% among those in a nonintensive group (Menon et al., 2016). Qualitative research conducted during the Lulun Project in Ecuador revealed cultural beliefs that eggs can cause gastrointestinal problems in young children and increase cholesterol (Waters et al., 2018). However, with provision of eggs and a social marketing campaign, egg consumption among young children over the course of 6 months increased 128% in the intervention group (from 40% to 91%) compared with only 33% in the control group (45% to 60%; Iannotti, Lutter, Stewart, et al., 2017). In rural Sichuan, China, an intervention that promoted giving young children a hard-boiled egg yolk resulted in a higher percentage of mothers in the intervention group reporting that egg yolk should be the first food for infants and 24-hr dietary recalls showed a significant increase in consumption by the young child (Guldan et al., 2000). However, the study also showed a wide gap between knowledge and behaviours; although 65% of mothers in the intervention group reported that egg yolk should be the first food given, only 37% actually gave it to their infants aged 4 to 6 months. No studies were found that promoted consumption of eggs among pregnant and lactating women.

Concerns about egg allergies in high-income countries resulted in complementary feeding guidelines that recommended delaying their introduction until after the first year likely also discourage giving eggs to young children elsewhere in the world. Since 2003, several authoritative guidelines have recommended the introduction of eggs at 6 months (Greer et al., 2008; PAHO/WHO, 2003) and a recent systematic review reported early introduction of eggs to be associated

with reduced egg allergy (Ierodiakonou, 2016). Notwithstanding, this information has yet to be reflected in complementary feeding guidelines in some low- and middle-income countries. This was also the case in Ecuador, though as a result of the Lulun Project, the Ministry of Public Health updated its feeding guidelines to recommend earlier introduction of eggs (Ministerio de Salud Publica de Ecuador, 2016).

Economic barriers that limit access are likely to be far more important than cultural ones in explaining low consumption of eggs among women and young children. Cost was the primary limitation to routine egg consumption in rural Zambia (Hong, Martey, Dumas, & Travis, 2016). Prior to an intervention that increased flock size and eggs production, households in rural Zambia sold eggs or chickens rather than for consumption (Dumas et al., 2016). A recent analysis showed that eggs are a very expensive source of calories in low-income countries with caloric prices of these foods very strongly associated with consumption patterns among young children (Headey & Hirvonen, 2017). Economic aspects poultry and eggs are the subject of the paper by Morris et al., in this supplement.

3 | DISCUSSION

The consumption of eggs during pregnancy, breastfeeding, and early childhood has the potential to improve birth outcomes, breast-milk composition, and child nutrition and brain development. At the same time, consumption by women of reproductive age and young children is low, especially for infants 6 to 8 months of age and in the African region. Although both cultural and economic reasons likely explain this, inasmuch as consumption increases with child age, it is likely that consumption among older infants could increase to at least that of young children as these households clearly have some access to eggs. This is especially important given that the Lulun Project found that daily consumption of eggs for 6 months starting at 6–9 months led to an increase in linear growth by a length-for-age z-score of 0.63 and a reduction of 47% in stunting as well as increases in biomarkers associated with cognitive development.

Given the relationship between socio-economic status and egg consumption, consumption is also likely to increase as household incomes rise. In India, consumption among breastfed children 6 to 23 months of age increased nearly threefold between DHS surveys conducted between 2005–2006 and 2015–2016, from 4.7% to 13.3% (an increase of 183%). In Cambodia, the percentage point increase between 2005 and 2014 was twofold, from 17.4% to 35.9%. In contrast, in Nepal, the percentage point increase was extremely modest, from only 9.5% in 1996 to 13.2% in 2016. Clearly, in addition to overall efforts to improve household incomes, efforts to increase egg availability and access are also needed.

Vegetarian populations may particularly benefit when religious beliefs do not preclude egg consumption. In India, one third of the 1.25 billion inhabitants are vegetarian. In the 2006–2006 DHS, egg consumption among Indian women of reproductive age who had given birth in the previous 3 years was only 3%, the lowest of any country for which nationally representative data exist. According to mother's report, 15% of newborns to have been smaller than average and 6% very small for a total of 21%.

Inasmuch as the consequences of poor nutrition not only have life-long consequences for a child but also for the economic development of a country (Kim, 2015), the potential contribution of eggs to brain development is particularly noteworthy. Eggs provide the most concentrated source of choline, which is essential for a myriad of processes critical for brain development. The unique egg matrix that includes macronutrients, micronutrients, and hormone and immune factors may act in concert to not only promote growth but also child development.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

CKL was responsible for conceptualizing the paper and writing most of the first draft. LLI wrote the section on brain development and commented on the paper. CSP reviewed and extensively commented on the paper.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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