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The Impact of Early Nutrition on Health: Key Findings from the Cebu Longitudinal Health and Nutrition Survey (CLHNS)

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ABSTRACT

Introduction: The Philippines' Cebu Longitudinal Health and Nutrition Survey (CLHNS) is one of the longest running birth cohort studies in Southeast Asia. This paper illustrates the pathways through which maternal and infant nutrition influence later health outcomes using selected CLHNS findings. **Methods:** The CLHNS initially examined the determinants and consequences of low birth weight and early nutrition on child growth and development. It has since expanded to study other health, nutrition, and demographic issues in the life course of the cohort participants such as the consequences of early nutrition on adult health. **Results**: CLHNS findings have documented important effects of poor maternal nutrition beyond impaired foetal growth (manifested through low birth weight). Mothers who had lower energy intakes and poorer nutritional status during pregnancy had offsprings who were at risk of having higher blood pressure measurements in adolescence. Infants born small at birth were not only more likely to be stunted through adolescence, but were also at greater risk of cardiovascular disease later in life. Among the males, those born thin at birth and have high BMI in adulthood had increased risk of elevated systolic blood pressure. Early infant feeding also had long-term effects on health. Breastfeeding not only protected against morbidity and stunting in childhood, but also lowered the risk of insulin resistance and high triglyceride levels in adulthood among the males. Delayed complementary feeding was associated a with lower risk of overweight in young adulthood. An intergenerational matrilineal effect was also observed among the participants, with maternal birth weight being positively associated with offspring birth weight. **Conclusion**: The CLHNS findings support the WHO recommendations for exclusive breastfeeding until six months, timely introduction of complementary foods, and continued breastfeeding until two years. Since child nutrition begins *in utero*, programs should focus on improving maternal nutrition during pregnancy to minimise the risk of low birth weight.

Keywords: Maternal nutrition, health, Cebu Longitudinal Health and Nutrition Survey, infant feeding

INTRODUCTION

There is growing evidence linking early nutrition with health outcomes beyond infancy and childhood, building on the work of Barker & Osmond (1986;1988) on foetal origins of adult disease. Also referred to as the developmental origins of health and disease (DOHaD), this research concept is based on the premise that poor nutritional environment *in utero* impairs foetal growth and results in physiologic changes and

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systemic malfunctions that predispose the fetus to later health problems (Adair & Dahly, 2004; Gluckman, Hanson & Pinal, 2005; Thompson, 2012; Victora *et al*., 2008; Wadhwa *et al*., 2009). Long-term consequences of early nutrition are best examined through longitudinal studies with data from gestation through adulthood. One such study is the Philippines' Cebu Longitudinal Health and Nutrition Survey (CLHNS), one of the longest-running birth cohort studies in Southeast Asia. Launched in 1983, this ongoing study was initially designed to examine the determinants and consequences of pregnancy outcomes, particularly low birth weight, and the impact of early nutrition on child growth and development. This multidisciplinary effort has since expanded its research focus to include determinants of adult health, and other relevant issues in the life course of the cohort participants. More details on the CLHNS and its collaborators can be found in Adair & Popkin (2001), Adair *et al.* (2011) and The Cebu Study Team (1991).

METHODS

The CLHNS research design

The CLHNS is an ongoing study based in Metro Cebu, the second largest metropolitan area in the Philippines. In 1983, participants were recruited from 33 *barangays* or villages (17 urban and 16 rural) that were randomly selected from all the *barangays* in Metro Cebu using single-stage cluster sampling. The initial sample area included urban, peri-urban, mountain, and island *barangays*, capturing a sample with sufficient heterogeneity in maternal/infant behaviours and outcomes. The CLHNS baseline survey recruited 3327 pregnant women in their last trimester of pregnancy who were due to give birth between May 1983 and April 1984. The birth survey was conducted within a week after these baseline women gave birth, identifying the 3080 singleton infants (53% males) that comprised the one-year birth cohort sample. These mothers and index children have been followed up through the first 2 years (12 bimonthly post-partum surveys between 1983 and 86), and in 1991, 1994, 1998, 2002, and 2005. Brief cohort tracking surveys were conducted in 2007 and 2009 (index children only). The 2009 survey has data on 1709 or 55% of the original birth cohort. Attrition in the CLHNS is mainly due to migration out of the Metro Cebu area.

During the birth survey, birth weight data were obtained with permission from the mothers, hospitals, or local midwives (for home births). Gestational ages were estimated based on the mothers' last menstrual period or through Ballard scores (for infants with low birth weights). Comprehensive data on breastfeeding and complementary feeding were collected in the post-partum surveys. Weight and length/height were obtained from the cohort participants at each survey; skinfold was measured starting in the 1991 survey. Maternal weight, height, and triceps skinfold were obtained in all surveys. From baseline through 2005 (except in 1991), dietary data were collected using the 24-hour food recall method (single day recall through 2002; 2-day recall starting in 2005). In 1991 a food frequency questionnaire was used. At each full survey, a core set of socio-demographic, environmental, morbidity, and health behaviour modules were administered . New questions are added to capture important milestones and topics relevant to the cohort's age group. For example, CLHNS started collecting blood pressure measurements and biological markers of chronic diseases (through saliva and blood samples) as the cohort reached adolescence and young adulthood respectively (see Adair *et al*., 2011 for full list of biospecimens collected). Data were collected by trained research teams through structured interviews and assessments conducted at the participants' homes. Mothers were the main respondents from

baseline through the 1994 survey, and thereafter separate mother and child interviews were conducted. The study design and data collection protocol for each CLHNS round were reviewed and approved by the Institutional Review Board, Office of Human Research Ethics of the University of North Carolina at Chapel Hill.

Intergenerational component

In 2009, the CLHNS started tracking pregnancies and births among the female cohort participants, patterned after the original baseline pregnancy and birth surveys. This ongoing survey adds an intergenerational component to the CLHNS providing a unique opportunity to examine determinants and consequences of pregnancy outcomes in three matrilineal generations and explore new avenues in developmental plasticity (Kuzawa, 2005; Kuzawa, 2007) .

Consortium of Health Orientated Research in Transitioning Societies (COHORTS)

Having observed the cohort through almost 30 years of socio-economic and environmental changes in the Philippines, CLHNS has likewise documented health implications of the nutrition and socio-economic transitions underway in the country. This makes the CLHNS cohort even more ideal for DOHaD analyses as the effects of foetal programming is premised to be more strongly observed in transitioning populations potentially exposed to a mis-matched nutritional environment: prenatal deficiency combined with nutrition excess in later life (Barker, 2006; Wadhwa *et al*., 2009). The CLHNS and four other birth cohort studies from transitioning societies (Pelotas Birth Cohort Study (Brazil), Institute of Nutrition of Central America and Panama Nutrition Trial Cohort (Guatemala), New Delhi Birth Cohort (India), and Birth-to-Twenty Study (South Africa)) formed COHORTS to examine DOHaD issues with the strength of pooled cohort data (Richter *et al*., 2012).

RESULTS AND DISCUSSION

Influence of early nutrition on later health outcomes: evidence from the CLHNS

This section features selected CLHNS findings that illustrate the pathways through which maternal and infant nutrition influence later health outcomes in this particular cohort (Figure 1). Several papers on the determinants and consequences of early nutrition have been published using the CLHNS data and reviewed elsewhere (Adair *et al*., 2011).

Effects of maternal nutrition on birth weight and infant size at birth

The effect of maternal nutrition on foetal growth, manifested through size at birth, has been supported by CLHNS findings. Adair & Popkin (1988) reported that maternal height (indicative of chronic nutritional status) and arm fat area during pregnancy (used as proxy for maternal fat reserves) were positively associated with infant's birth weight and length. Infants born proportionately small (using Rohrer's index (weight x100)/length^3)), reflecting poor maternal nutrition throughout pregnancy, were more likely to have mothers who were shorter and with lower maternal fat reserves. Among adolescent mothers at baseline, pregnancy weight-for-height and maternal fat reserves predicted infants' birth weight and gestational age, after controlling for maternal age and socio-economic variables (Borja & Adair, 2003).

Long-term influence of maternal nutrition

Maternal nutrition indirectly influences child growth through its effects on size at birth. Low birth weight (LBW) infants (<2500 gms) were more likely to be small at age one. Infants born proportionately small had larger weight and length deficits Adair (1989). Close to 70% of the cohort were stunted by age two, with about half of the sample remaining stunted in adolescence.

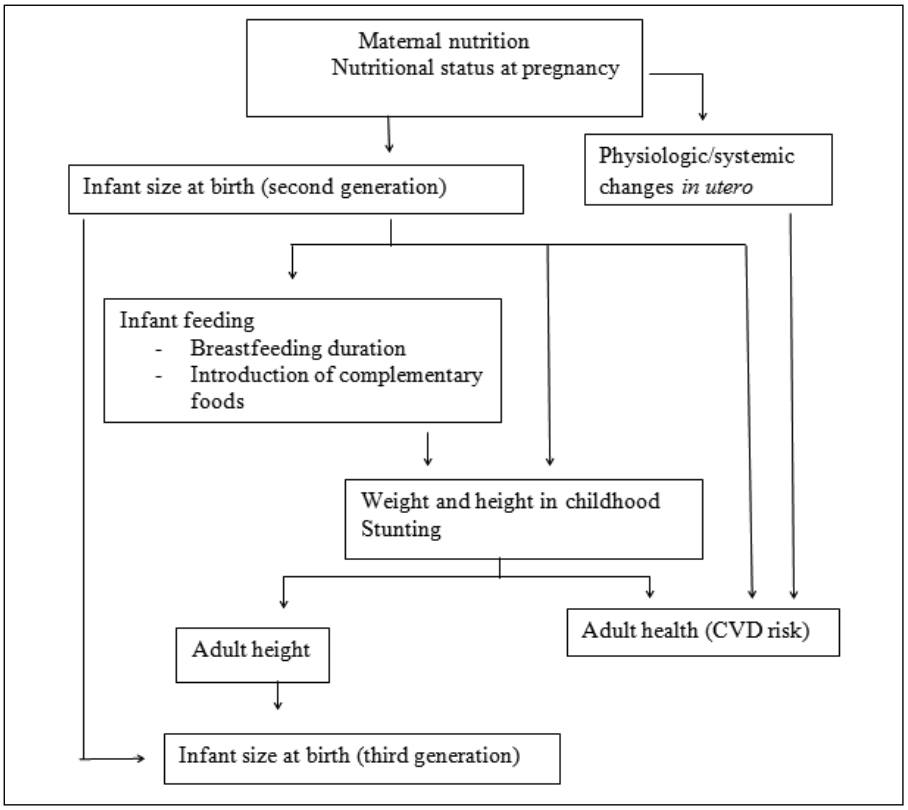

Figure 1. Short- and long-term consequences of early nutrition

LBW appeared to be a strong predictor of stunting. Independent of its effect on birth weight, maternal height was negatively associated with stunting, (Adair & Guilkey, 1997).

The long-term influence of maternal nutrition during pregnancy on health was first observed when the cohort reached adolescence. Among the males, systolic blood pressure (SBP) was inversely associated with maternal height and mother's per cent energy intake from protein. Lower fat reserves during pregnancy (based on triceps skinfold measurements) were associated with higher SBP and diastolic blood pressure (DBP). In females, lower maternal energy intakes from fat were associated with higher SBP and DBP (Adair, Kuzawa, & Borja, 2001). These findings support the hypothesis that poor maternal nutrition prior to and during pregnancy may cause systemic changes *in utero* that alter blood pressure regulation in later life (Adair & Dahly, 2005).

Effects of infant feeding practices on child health and development

The majority of the cohort (95%) were ever breastfed with a mean breastfeeding duration of 13.3 months. About 28% of infants were breastfed until 12-18 months. A higher proportion of children from rural areas were ever breastfed (and breastfed longer) compared to those in urban areas (Popkin *et al.*, 1990); Zohoori, Popkin & Fernandez, 1993). Table 1 shows breastfeeding patterns within the first two years. Mean age of introduction of semi-

Table 1. Breastfeeding patterns among CLHNS mothers within the first 2 years (shown here as percentages).*

	Prevalence (%)			
Breastfeeding pattern	*2 months (n=2886)*	*4 months (n=2806)*	*6 months (n=2720)*	*12 months (n=2600)*
Exclusive breastfeeding	31.1	20.1	3.2	0.1
Any breastfeeding	53.3	59.4	70.7	61.9
No breastfeeding	15.7	20.3	24.0	38.0

* Modified from Popkin *et al.* (1990)

solid/solid foods was 4.5 months. About 82% of the infants started complementary feeding between 3-6 months of age (Fall *et al.*, 2011). Shifts in infant feeding patterns were observed among mothers. Infants may be mixed fed at 2 months then exclusively breastfed at 4 months, suggesting that the transition from breastfeeding or formula feeding to full supplemental feeding may take a complex route (Bisgrove, Popkin & Barba, 1991).

The decision to breastfeed was influenced by the mother's perception of how well the infant was growing. Adair & Guilkey (1997) reported that LBW infants were less likely to be breastfed and more likely to be weaned earlier. It was noted that mothers of LBW infants who intended to breastfeed during the baseline pregnancy interview ended up not breastfeeding after delivery. One possible explanation for this behaviour was the absence of breastfeeding promotion programmes during the 1980s, when baseline interviews were conducted. During this period, a significant proportion of mothers believed that formula feeding was superior to breastfeeding. Subsequently, mothers who perceived their infants as thin were more likely to stop breastfeeding sooner and shift to formula feeding (Adair & Popkin, 1996).

CLHNS papers have been written on the effects of breastfeeding against infant morbidity, particularly of its protective effect against diarrhea even in pathogenic environments (Vanderslice, Popkin & Briscoe, 1994; The Cebu Study Team, 1991; Popkin *et al.*, 1990). Compared to exclusively breastfed infants, those fed both breastmilk and other liquids (including other milks) had 2-3 times greater risk of having diarrhea (Popkin *et al.*, 1990).

Breastfeeding was associated with a lower risk of stunting among CLHNS children in a model controlling for birth weight, maternal height, infant gender, energy intake, and morbidity variables. The effect was strongest in the first 12 months. On the other hand, infant energy intake from supplemental foods within the first year (particularly 0-6 months) was associated with a higher risk of stunting (Adair & Guilkey, 1997).

Size at birth, infant feeding and cardiovascular risk in adulthood

Pooled analysis of COHORTS data showed that, after adjusting for adult BMI, birth weight was negatively associated with adult blood pressure, and the odds of pre-hypertension. The findings further showed that timing of catch-up growth has important implications. Weight gained in later childhood was positively associated with blood pressure readings particularly among those born small for gestational age (Adair *et al.*, 2009). Among the CLHNS male cohort participants, poor foetal nutrition (i.e., being born thin at birth) combined with weight gain in adulthood increased the risk of elevated adult SBP (Adair & Cole, 2003).

These findings lend further support to the pre-and postnatal mismatch hypothesis where systemic malfunctions (e.g. to the renal system) due to poor nutrition *in utero* make it difficult for the body to handle nutrient excesses in later life.

Longer breastfeeding duration protected second-generation adult males against insulin resistance and high triglyceride levels (Lee, Borja & Adair, 2009). In addition, delayed introduction of complementary foods was associated with lower body mass index, waist circumference, and per cent body fat measures in adulthood (Fall *et al.*, 2011). Thompson (2012) offers several potential mechanisms linking early feeding to risk of adult obesity. The macronutrient composition and bioactive components of breast milk provide for better appetite and weight regulation. These protective mechanisms are disrupted with early introduction of complementary feeding.

Maternal birth weight influences offspring birth growth

Kuzawa & Eisenberg (2012) examined the influence of the cohort's birth weight on reported birth weight of their own offspring (third generation). Multivariate models show that a 1 kg change in maternal birth weight predicts a mean increase of 271 g in offspring birth weight. The influence of paternal birth weight was lower (mean increase of 132 g) indicating a stronger matrilineal influence on foetal growth. Thus, for mothers born with low birth weights, the disadvantage of being born small extends to the next generation, potentially triggering a cycle of poor growth during infancy and poor health through adulthood.

Study limitation

Sample selectivity, brought about by attrition, is the major limitation of the CLHNS. Participants who continue to be in the study are more likely from rural, higher-parity, and lower socio-economic status households.

CONCLUSION

The CLHNS findings reinforce the message that the crucial period for infant nutrition begins in pregnancy. Poor foetal nutrition, as manifested through size at birth, is associated with poor adult health. Continued efforts to ensure proper nutrition during pregnancy to minimise the risk of low birth weight are recommended. The importance of proper infant feeding on health, not only during infancy but through adulthood, is particularly highlighted in this study. The CLHNS findings support the WHO recommendations for exclusive breast-feeding up to 6 months, timely introduction of complementary foods (not earlier than 6 months), and continued breastfeeding until two years.

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