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# Catch-up growth in Malawian babies, a longitudinal study of normal and low birthweight babies born in a malarious endemic area

B.F. Kalanda<sup>a,b</sup>, S. van Buuren<sup>c</sup>, F.H. Verhoeff<sup>a</sup>, B.J. Brabin<sup>a,d,\*</sup>

<sup>a</sup>Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Liverpool, UK <sup>b</sup>College of Medicine, University of Malawi, Blantyre, Malawi <sup>c</sup>Department of Statistics, TNO Prevention and Health, Leiden, The Netherlands <sup>d</sup>Emmakinderziekenhuis, Academic Medical Centre, University of Amsterdam, The Netherlands

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KEYWORDS	Abstract
Birthweight; Malawi; Malaria	<ul> <li>Introduction: Infant growth has not been studied in developing countries in relation to maternal factors related to malaria in pregnancy and maternal illiteracy.</li> <li>Objective: To describe growth patterns in infants with low and normal birthweight and determine maternal risk factors for infant undernutrition.</li> <li>Methods: Babies born in a rural district of southern Malawi were recruited. An infant cohort was selected on the basis of low or normal birthweight. Weight and length were recorded at birth and at 4-weekly intervals until at 52 weeks after birth. Maternal characteristics at first antenatal attendance and delivery were obtained. Odds ratios in univariate analysis were adjusted for birthweight. Factors included in the multivariate regression included maternal illiteracy, season of birth, maternal iron deficiency and number of infant illness episodes.</li> </ul>
	<i>Results:</i> Low birthweight infants were shorter and lighter throughout infancy than either normal birthweight or international reference values. At 12 months, placental or peripheral malaria at delivery (adjusted odds 1.8; 1.0, 3.1), number of infant illness episodes (AOR=2.1; 1.2, 3.6) and maternal illiteracy (AOR=2.7; 1.5, 4.9) were independently associated with low weight for age. Maternal short stature (AOR=1.8; 1.1. 3.2), male sex (AOR=2.4; 1.4, 4.1), number of infant illness episodes (AOR=2.6; 1.5, 4.4), and birth in the rainy season (2.1; 1.2, 3.7) were independently associated with stunting. Placental or peripheral malaria at delivery (AOR=2.2; 1.1,

\* Corresponding author. Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, England, UK. Tel.: +44 151 708 9393; fax: +44 151 705 3370.

E-mail address: b.j.brabin@liverpool.ac.uk (B.J. Brabin).

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4.4) and number of illness episodes (AOR=2.2; 1.1, 4.5) were independently associated with thinness.

*Conclusion:* Malaria during pregnancy and maternal illiteracy are important maternal characteristics associated with infant undernutrition. Innovative health/literacy strategies are required to address malaria control in pregnancy in order to reduce the magnitude of its effects on infant undernutrition.

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## 1. Introduction

Due to poor weaning practices and the low nutritional value of food, linear growth restriction is common in less developed countries [1]. Appropriate child growth is of public health importance because poor weight gain has been associated with cot death [2], developmental delay [3] and disease in adults [4]. In developing countries, poor childhood growth can signify parasitic infection [5,6], repeated bacterial or HIV infection [7,8], or a poor psychological state in the mother and/or child [9,10].

International or local reference growth curves are used for comparison of growth percentiles between populations. The consensus is for international reference comparisons [11,12], on the basis that growth potential is similar among different human populations with access to adequate nutrition and no unusual burden of infection. Local reference curves have been recommended to identify individuals at risk within a specific group, but not to assess the degree to which they are reaching their growth potential [13,14].

Low birthweight (LBW) babies are often smaller during infancy [15] but with high energy feeding, many show catch up growth in the first years of life [16]. In developing countries, the growth of LBW babies has not been evaluated to identify "catchup" growth to the same extent as in western populations [17]. There is little data available which compares their growth patterns with international reference values.

The aims of this analysis were to compare the growth patterns of Malawian low birthweight and normal birthweight infants against international reference values, and to determine factors associated with poor infant growth at 6 and 12 months of age.

## 2. Methods

#### 2.1. Study area

This study was undertaken between March 1993 and July 1995 in Chikwawa District, in the lower shire

valley, south of Malawi. This is a rural area where malaria transmission is endemic. The average rainfall in the study period was 520 mm/year of which 88% fell in the months of November—March. Small-scale agriculture of maize, sorghum, cotton and sugar cane are the primary source of food and income. The study was located in the two hospitals in the District, Chikwawa District Hospital (CDH), a government hospital with free services and Montfort Hospital (MH), 30 km away, which is a feepaying mission hospital.

## 2.2. Enrolment

All women attending the antenatal facilities were screened at their first antenatal visit after verbal consent was obtained. A questionnaire, completed by a project nurse, included information on age and obstetric history. Maternal weight, in bare feet, to the nearest kilogram was measured (SECA scale) and height to the nearest centimetre. Midupper-arm-circumference was measured at the mid-point of the right arm (nearest 0.1 cm). Maternal literacy was assessed by requesting the mother to read a simple sentence in the local language, Chichewa.

#### 2.3. Delivery

Information on delivery was only collected from women who attended the hospital facilities of CDH or MH for delivery. For logistic reasons, it was not possible to obtain this information from home or health centre deliveries. Birthweight was measured immediately after birth on a Salter scale to the nearest 10 g and the baby was examined for gestational age between 6 and 24 h after delivery using a modified Ballard method [18]. Women stayed 48 h postpartum in hospital for observation. A venepuncture blood sample was collected from women before delivery and from the cord and placenta for measurement of haemoglobin, free erythrocyte protoporphyrin and MCHC. A malaria slide was made from blood collected deep between the placenta villi. Malaria slides were stained with Giemsa and read counting asexual



**Figure 1** P10, P50, P90 weight for age centiles for LBW and NBW infants (combined sexes) compared with P10, P50 CDC 2000 reference (- - - CDC; — NBW; ····· LBW).

*Plasmodium falciparum* parasites against 200 white blood cells. HIV status of women was determined using two different enzyme linked immunosorbent assays (ELISAs). The assays used were ICE\*HIV-1.0.2 (Murex; Dartford, UK) and for confirmation, VIDAS HIV-2 new test (bioMerieux; Lyon, France). This procedure was in accordance with WHO recommendations for the diagnosis of HIV infection in asymptomatic patients in regions where prevalence is higher than 10%. Pre- and post-test counselling was provided by trained nurses.

#### 2.4. Infant follow-up

A stratified sample of infants was selected based on low birthweight and controls born on the same day with normal birthweight. Babies who died within 48 h postpartum, during the hospital observation period, were excluded. To allow for seasonal factors, enrolment occurred over a 1-year period. Mothers were asked to return to the hospital with their child at 4-weekly intervals and visits were integrated with the immunisation schedule, consequently the first scheduled visit was at 6 weeks of



Figure 2 P10, P50, P90 length for age centiles for LBW and NBW infants (combined sexes) compared with P10, P50 CDC 2000 reference (- - - - CDC; —— NBW; · · · · · LBW).

life. An active surveillance system was in place to enhance follow-up for non-attendees. At each scheduled visit, weight in kilograms and length and head circumference in centimetres were recorded for each child and a morbidity questionnaire was completed.

## 2.5. Definitions

A cord haemoglobin of less than 12.5 g/dl was used as the cut-off value for fetal anaemia [19]. Preterm was defined as gestation less than 37 weeks at delivery, and low birthweight as <2500 g. The reference population was the CDC 2000 reference with combined sex values [20]. Underweight was defined as weight for age (W/A) $\leq$ -2S.D., stunting as length for age (L/A) $\leq$ -2S.D. and thinness as weight for length (W/L) $\leq$ -2S.D. [11]. Intrauterine growth restriction (IUGR) was defined as weight below the 10th percentile of the birthweight for gestational age, sex-specific risk curve [21] as recommended by WHO [11]. Severe maternal anaemia was Hb less than 8 g/dl, iron deficiency as a combination of free erythrocyte protoporphyrin (FEP)>3.1  $\mu$ g ZPP g/Hb [22] and MCHC<32.0% [23]. A MUAC<23 cm [11], BMI<18.5 kg/m<sup>2</sup> [24] or



Figure 3 Infant mean Z-scores (W/A, L/A, W/L) for LBW and NBW infants (combined sexes); NBW (-----); LBW (----).

weight <50 kg were considered as maternal undernutrition and height <150 cm as short stature [25]. Maternal weight was only included if measured before 18 weeks gestation.

## 2.6. Analysis

Logistic regression was used to analyse risk factors related to low anthropometric indices. Factors included in multivariate regression were those that were significant (p < 0.05) in univariate analysis, and also pre-term birth, IUGR and malaria at delivery as these are well established correlates of low birthweight risk. Odds ratios in univariate and multivariate analysis were adjusted for birthweight since subjects were selected by birthweight status and to correct for regression to the mean. Growth curves were drawn in Excel using smoothed percentile standards derived by the LMS program [26] version 1.16 (2000). Standard deviation scores were calculated using the EPI Info 2002, nutrition program. This uses the CDC 2000 reference as the standard [20].

# 2.7. Ethical approval

The study was granted ethical approval by the Malawi College of Medicine Research and Ethics Committee (COMREC).

## 3. Results

A total of 4104 women attended the first antenatal visit, of whom 1523 (37.1%) delivered in hospital. Among 561 infants recruited, 67 babies did not attend for any visit and birthweight was not recorded for 24 babies who were excluded. There were 147 infants with low birthweight and 323 with normal birthweight. Males comprised 50.5% of the sample. There were a total of 4888 months of follow-up for 470 infants, with a median follow-up period of 11 months. There were a total of 5094 weight and length measurements. During the follow-up period, 39 infants died, 4 in the first month, and the remainder evenly throughout the postneonatal period [27].

Figs. 1 and 2 show the weight for age (W/A) and length for age (L/A) curves for Malawian LBW and NBW babies compared with the CDC 2000 reference. Fetal anaemia had no significant effect on infant weight or length during the follow-up period. Malawian infants were shorter and lighter compared to the CDC 2000 reference. The size of this difference in P50 increased during the first year of life in NBW infants from 1.4 to 4.3 cm for length, and from 0.40 to 1.70 kg for weight (both p < 0.05). For LBW infants, the corresponding differences over the first year of life were 4.3 to 6.0 cm for length, and 1.3 to 2.4 kg for weight (both p < 0.05).

Table 1Univariate analysis of maternal and infant characteristics associated with low W/A scores (<-2S.D.) at 6</th>and 12 months

Characteristic	6 months OR (95% C.I.)	12 months OR (95% C.I.)
Sex (male)	1.46 (0.83, 2.57) (322)	1.21 (0.75, 1.96) (318)
Illiterate	4.72 (1.93, 11.53) <sup>a</sup> (320)	2.71 (1.55, 4.73) <sup>a</sup> (317)
Maternal anaemia at delivery	1.47 (0.70, 3.09) (316)	1.18 (0.58, 2.41) (312)
Maternal anaemia at recruitment	1.31 (0.69, 2.47) (295)	0.88 (0.50, 1.54) (292)
Maternal HIV infection	1.83 (0.98, 3.42) (315)	1.09 (0.63, 1.90) (311)
Parity (Primigravidae)	0.67 (0.35, 1.29) (320)	0.67 (0.38, 1.17) (317)
Season of birth (rainy season)	1.91 (1.05, 3.47) (321)	1.17 (0.71, 1.92) (318)
Malaria at delivery <sup>b</sup>	1.22 (0.68, 2.20) (314)	1.66 (0.99, 2.81) (312)
Malaria at recruitment	1.39 (0.73, 2.66) (305)	0.71 (0.38, 1.30) (305)
Pre-term delivery (<37 weeks)	1.87 (0.97, 3.61) (319)	0.80 (0.41, 1.56) (316)
IUGR	1.16 (0.60, 2.24) (319)	1.37 (0.75, 2.50) (316)
Fe def. <sup>c</sup> (recruitment)	2.72 (1.52, 4.85) <sup>a</sup> (318)	1.49 (0.88, 2.54) (314)
Fe def. (delivery)	1.50 (0.82, 2.72) (285)	1.14 (0.68, 1.90) (283)
SP (x1 vs. x2) <sup>d</sup>	2.25 (0.82, 6.20) (118)	1.04 (0.46, 2.32) (117)
Short stature (<150 cm)	0.92 (0.36, 2.35) (318)	2.60 (0.96, 7.02) (315)
MUAC<22 cm	1.08 (0.18, 6.34) (304)	0.19 (0.03, 1.35) (304)
Weight at recruitment (<50 kg)	1.70 (0.95, 3.06) (320)	1.55 (0.92, 2.61) (316)
Number of illness episodes (>5)	1.73 (0.96, 3.12) (302)	2.10 (1.26, 3.49) <sup>a</sup> (302)
Early weaning (<3months)	1.33 (0.75, 2.35) (319)	1.49 (0.91, 2.45) (316)

The univariate analysis is adjusted for low birthweight to correct for regression to the mean.

Brackets: sample size.

<sup>a</sup> Significant, *p*<0.05.

<sup>b</sup> Placental or peripheral malaria at delivery.

<sup>c</sup> Iron deficiency anaemia.

 $^{\rm d}\,$  SP: one versus two doses of sulfadoxine pyrimethamine; Fe, iron.

### 3.1. Standard deviation (S.D.) scores

Fig. 3 illustrates the mean Z-scores calculated from the CDC references for W/A, L/A and weight for length (W/L) for the combined sexes for the two birthweight categories. Throughout infancy, mean Z-scores of low birthweight babies remained negative, and were always below the -1S.D. score for both W/A and L/A. There was no evidence of catchup growth after 18 weeks of age. The S.D. scores for W/A and L/A remained parallel for babies of both birthweight categories throughout infancy. For W/L, an increasing difference between LBW and NBW infants was present after 18 weeks of age.

#### 3.2. Univariate and multivariate analysis

#### 3.2.1. Underweight

The relative risk as estimated by odds ratio of underweight for LBW compared to NBW babies at 6 months was 3.1 (95% C.I. 1.8, 5.5), and even higher at 12 months 4.8 (2.8, 8.3). Maternal and infant factors associated with underweight at 6 and 12 months are summarised in Table 1. Maternal illiteracy, season of birth and iron deficiency at recruitment were the most significant factors associated with infant undernutrition at 6 months of infancy, and at 12 months these were maternal illiteracy and number of illness episodes during infancy.

Table 2 summarises a multivariate analysis which included significant factors identified in the univariate analysis. A number of characteristics remained strongly associated with W/A of less than -2S.D. Maternal illiteracy had the highest adjusted odds ratio at 5.58 for the 6 months growth analysis (p<0.001). This also remained significant at 12 months. Maternal malaria at delivery was associated with low W/A at both 6 and 12 months.

#### 3.2.2. Stunting

There was an increased risk of stunting in LBW babies at 6 months (5.1, 95% C.I. 2.9, 8.8). At 12 months, the risk was 2.3 (1.4, 3.8). Table 3 summarises factors associated with infant stunting at 6 and 12 months. Significant risk factors at 6 months included maternal illiteracy, iron deficiency at recruitment, pre-term birth and number of infant illness episodes. At 12 months the corresponding factors were maternal illiteracy and short stature, season of birth, male sex and number of infant illness episodes.

In multivariate analysis, LBW (AOR=4.5; 2.3, 8.9), pre-term delivery (AOR=2.2; 1.1, 4.5), maternal iron deficiency anaemia at recruitment

Table 2 Adjusted odds ratios for factors associated with low infant W/A, L/A, and W/L

	Adjusted OR	95% C.I.	p-value
6 months			
Weight for age (W/A)			
Illiterate	5.6	2.2, 14.0	<0.01
Pre-term delivery	3.1	1.6, 5.9	0.01
Iron deficiency anaemia at recruitment	2.7	1.5, 4.9	0.02
IUGR	2.4	1.3, 4.6	0.01
Length for age (L/A)			
LBW	4.5	2.3, 8.9	<0.01
Number of disease episodes	3.3	1.7, 6.3	<0.01
Pre-term delivery	2.2	1.1, 4.5	0.03
Iron deficiency anaemia at recruitment	2.1	1.1, 4.1	0.03
Weight for length (W/L)			
Illiterate	3.5	1.0, 11.8	0.05
Season of birth (rainy)	0.3	0.1, 0.8	0.01
12 months			
Weight for age (W/A)			
LBW	6.1	3.3, 11.5	< 0.01
Illiterate	2.7	1.5, 4.9	0.01
Number of illness episodes	2.1	1.2, 3.6	0.01
Malaria at delivery <sup>a</sup> Length for age (L/A)	1.8	1.0, 3.1	0.05
Weight ( $<50 \text{ kg}$ )	1.8	1.1.3.2	0.03
Season of birth (rainy)	2.1	1.2. 3.7	0.01
Sex (male)	2.4	1.4.4.1	0.01
Number of infant	2.6	1.5.4.4	< 0.01
illness episodes		,	
Weight for length (W/L)			
Malaria at deliverv <sup>a</sup>	2.2	1.07.4.4	0.03
Number of illness	2.2	1.1 4.45	0.03
episodes			0.00

<sup>a</sup> Placental or peripheral malaria.

(AOR=2.1; 1.1, 4.1) and number of infant morbidity episodes (AOR=3.3; 1.7, 6.3) were independently associated with low L/A at 6 months (Table 2). At 12 months, maternal weight (AOR=1.8; 1.1, 3.2), season of birth (AOR=2.1; 1.2, 3.7), male sex (AOR=2.4; 1.4, 4.1) and number of infant illness episodes (AOR=2.6; 1.5, 4.4) were independently associated with low L/A.

#### 3.2.3. Thinness

At both 6 and 12 months, LBW babies showed no increased risk for low W/L, 1.4 (0.6, 3.2) and 1.5 (0.8, 3.1) compared to NBW infants. In univariate analysis, malaria at recruitment was associated with thinness at 6 months (2.37; 1.04, 5.04) and malaria at delivery with thinness at 12 months (2.25; 1.12, 4.51). Maternal illiteracy was marginally associated with this outcome at 6 and 12 months.

Characteristic	6 months OR (95% C.I.)	12 months OR (95% C.I.)			
Sex (male)	1.54 (0.86, 2.75) (322)	2.57 (1.57, 4.21) <sup>a</sup> (321)			
Illiterate	2.18 (1.05, 4.55) <sup>a</sup> (321)	2.28 (1.28, 4.06) <sup>a</sup> (320)			
Maternal anaemia at delivery	1.75 (0.83, 3.70) (316)	1.15 (0.58, 2.26) (315)			
Maternal anaemia at recruitment	1.15 (0.61, 2.20) (294)	0.75 (0.43, 1.30) (294)			
Maternal HIV infection	1.74 (0.91, 3.32) (316)	1.05 (0.60, 1.81) (314)			
Parity (Primigravidae)	0.67 (0.35, 1.29) (321)	0.94 (0.55, 1.62) (320)			
Season of birth (rainy season)	1.45 (0.80, 2.65) (322)	1.88 (1.13, 3.13) <sup>a</sup> (321)			
Malaria at delivery <sup>b</sup>	0.87 (0.43, 1.74) 0.88	1.20 (0.72, 1.99) (315)			
Malaria at recruitment	0.87 (0.43, 1.74) (306)	0.89 (0.49, 1.62) (306)			
Pre-term delivery (<37 weeks)	2.00 (1.04, 3.87) <sup>a</sup> (320)	1.32 (0.72, 2.43) (319)			
IUGR	0.78 (0.39, 1.55) (320)	0.84 (0.46, 1.51) (319)			
Fe def. <sup>c</sup> (recruitment)	2.09 (1.15, 3.82) <sup>a</sup> (319)	0.91 (0.54, 1.54) (317)			
Fe def. (delivery)	1.27 (0.69, 2.33) (285)	0.99 (0.59, 1.65) (285)			
SP (x1 versus x2) <sup>d</sup>	1.77 (0.69, 4.55) (120)	0.78 (0.36, 1.69) (119)			
Short stature (<150 cm)	2.02 (0.86, 4.78) (319)	2.82 (1.21, 6.57) <sup>a</sup> (318)			
MUAC<22 cm	1.76 (0.32, 9.69) (305)	0.66 (0.10, 4.24) (305)			
Weight at recruitment (<50 kg)	1.67 (0.92, 3.04) (321)	1.67 (1.01, 2.77) <sup>a</sup> (319)			
Number of illness episode (>5)	2.89 (1.56, 5.34) <sup>a</sup> (304)	2.35 (1.43, 3.88) <sup>a</sup> (304)			
Early weaning (<3 months)	1.01 (0.56, 1.83) (320)	1.45 (0.89, 2.36) (319)			

**Table 3** Univariate analysis of maternal and infant characteristics associated with low L/A scores (<-2S.D.) at 6 and 12 months

The univariate analysis is adjusted for low birthweight to correct for regression to the mean.

Brackets: sample size.

<sup>a</sup> Significant, p < 0.05.

<sup>b</sup> Placental or peripheral malaria at delivery.

<sup>c</sup> Iron deficiency anaemia.

 $^{\rm d}\,$  SP: one versus two doses of sulfadoxine pyrimethamine; Fe, iron.

In a multivariate analysis, at 6 months, birth in the rainy season (AOR=0.3; 0.1, 0.8) and illiteracy (AOR=3.5; 1.0, 11.8) were independently associated with low W/L (Table 2). At 12 months, malaria at delivery (AOR=22; 1.1, 4.4) and number of illness episodes (AOR=2.2; 1.1, 4.5) were significantly associated with low W/L.

# 4. Discussion

This is one of the few studies which has assessed the effect of non-nutritional factors on growth throughout infancy in low and normal birthweight babies using longitudinal data. Some authors have examined socioeconomic factors, which in various ways are a proxy for nutritional status and there is a large body of knowledge on infection and protein-energy malnutrition during infancy [28-30]. Few studies have examined the association of maternal characteristics at delivery and growth in infancy. In a study in Brazil, Ashworth et al. [31] surmised that early differential growth patterns were set in utero and were indirectly affected prenatally by socioeconomic status. Kolsteren et al. [32] also showed that growth deceleration in the first month in children from Madura, Indonesia, was related to intrauterine growth. This places emphasis on evaluation of maternal characteristics during pregnancy in relation to growth patterns during infancy.

This analysis shows that low birthweight babies were lighter and shorter throughout infancy and that catch-up in weight or length did not occur (Figs. 1-3). Selection bias may have occurred to the extent that only babies born in hospital were studied. A separate recent study of hospital and home deliveries in this area has shown no significant differences in birthweight outcomes between these two categories of delivery [33]. All babies, independent of birthweight category, were lighter and shorter than the CDC 2000 reference population for most of the first year of life. The exception was for W/L measurements during the first 3 months of infancy. Growth falters between 3 and 4 months as previously described in many studies from developing countries [34,35]. It is likely that low birthweight significantly contributed to this faltering, although the rate of faltering in weight after 10 weeks of age was similar for both birthweight categories. Healthy breast fed babies are known to weigh less than non-breast fed babies and this would explain the lower Malawian growth percentiles than the CDC reference values particularly later in infancy [36]. However the extent of fall-off in Malawian percentile values exceeds that attributable to breast feeding practice.

Figs. 1 and 2 show that the 10th percentile for W/A and L/A for low birthweight infants was lower than the 3rd percentile of the CDC reference throughout infancy. From about 5 months of age, the 10th percentile for W/A and L/A for normal birthweight infants was also lower than the 3rd percentile of the CDC reference.

At 12 months, low birthweight and malaria at delivery were independently associated with low W/A. Malaria in pregnancy alters utero-placental exchange of nutrients [37,38], which may lead to fetal growth restriction, or pre-term birth and reduce fetal stores of essential nutrients. Placental malaria also has been significantly associated with increased risk of fetal and infant anaemia [39,40].

At 6 months, IUGR and pre-term delivery were both associated with low W/A. Since both IUGR and pre-term delivery have been associated with maternal malaria [41,42], it is likely that a causal path for poor infant growth is through pregnancy malaria, pre-term-low birthweight and/or IUGR-low birthweight and impaired growth throughout infancy. The results from the present study show the close association between maternal malaria and undernutrition in infants at 6 and 12 months.

Low birthweight babies may experience greater morbidity leading to poor growth. The incidence of malaria, respiratory infections, diarrhoea and other episodes of morbidity was approximately 6 episodes per child per year in this cohort [43] and this infant morbidity is likely to have contributed to growth faltering. The association of undernutrition with the rainy season is probably explained by the higher incidence of diarrhoea and malaria during the rainy months. The number of infant illness episodes was significantly associated with undernutrition in weight, length and weight for length at 12 months. In rural Guatemala, Matorell et al. [44] showed that the increased frequency of illness was an important determinant of growth deficits and Cole [45], as well as others in The Gambia, demonstrated that respiratory and diarrhoeal infection reduced weight gain by 17 and 69 g/day respectively. In northeast Brazil, Ashworth et al. [31] reported that neonatal illness explained 3.1% of deficits in L/A Z-scores.

Maternal HIV was not independently associated with poor growth in this analysis. This may be because HIV status was not diagnosed in infants but in mothers, and the majority of infants would not have been HIV infected. In the European Collaborative study, HIV infected infants had poorer growth than uninfected infants [8]. In Brazil, HIV infected infants also had lower W/A, L/A and W/L from 3 to 21 months, although L/A was not affected at 3 months [46].

Maternal short stature and illiteracy were associated with low W/A and L/A. Short stature, or linear growth restriction, has been proposed as a proxy indicator for poverty in the mother's family [44]. Illiteracy is also an indicator of poor socioeconomic status as illiterate mothers are likely to be poor and have less access to healthy foods. There is little information on the association of literacy with child health and survival, and there are no prospective studies of literacy interventions and their effects on child growth. Poor maternal education has been shown to be a key characteristic related to child mortality [47]. This study is one of the first to determine the close association of poor maternal literacy with childhood undernutrition. Innovative strategies are required to address the problem of maternal illiteracy in these communities with a focus on combined health, nutritional and literacy interventions.

## 5. Conclusion

This analysis has shown that LBW babies do not catch-up in growth as reported in studies from developed countries. Malawian babies are shorter and lighter in comparison to the CDC 2000 reference values and maternal malaria at delivery was negatively associated with infant growth. Maternal illiteracy was highly significantly associated with infant undernutrition and should be reduced through formal and non-formal education programs. It is imperative that maternal and child health programs also implement interventions which improve malaria control in pregnancy in order to reduce LBW.

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#### References

 Simondon KB, Simondon F, Cornu A, Delpeuch F. The utility of infancy weight curves for the prediction of linear growth retardation in pre-school children. Acta Paediatr Scand 1991;80:1-6.

- [2] Sinclair-Smith C, Dinsdale F, Emery J. Evidence of duration and type of illness in children found unexpectedly dead. Arch Dis Child 1976;51:424-9.
- [3] Dowdney L, Skuse D, Heptinstall E, Puckering C, Zur-Szpiro S. Growth retardation and developmental delay among inner-city children. J Child Psychol Psychiatry Allied Discipl 1987;28:529-41.
- [4] Barker DJP, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. Lancet 1989;i:577-80.
- [5] ter Kuile FO, Terlouw DJ, Kariuki SK, Phillips-Howard PA, Mirel LB, Hawley WA, et al. Impact of permethrin-treated bed nets on malaria, anaemia, growth in infants in an area of intense perennial malaria transmission in western Kenya. Am J Trop Med Hyg 2003;68(4 Suppl.):68-77.
- [6] Sackey ME, Weigel MM, Armijos RX. Predictors and nutritional consequences of intestinal parasitic infections in rural Ecuadorian children. J Trop Pediatr 2003;49(1): 17-23.
- [7] Steketee RW. Pregnancy, nutrition and parasitic diseases. J Nutr 2003;133(5 Suppl. 2):16615-75.
- [8] Newell ML, Borja MC, Peckham C. European Collaborative study. Height, weight and growth in children born to mothers with HIV-1 infection in Europe. Pediatrics 2003; 111(1):e52-60.
- [9] Rahman A, Lovell M, Harrington R, Bunn J, Iqbal Z. Mother's mental health and infant growth: a case-control study from Rawalpindi, Pakistan. Child Care Health Dev 2004;30:21-7.
- [10] Whitehead RG. Growth in weight and length. Acta Paediatr 2003;92:406-10.
- [11] World Health Organisation. Physical Status: The use and interpretation of anthropometry. A Report of a WHO Expert Committee. WHO Technical Series Report 854. Geneva, 1995a.
- [12] Vaughan V. On the utility of growth curves. JAMA 1992;267(7):975-6.
- [13] Yip R, Scanlon K, Trowbridge F. Improving growth status of Asian refugee children in the United States. JAMA 1992; 267(7):937-40.
- [14] Janes MD, Macfarlane SBJ, Moody JB. Height and weight growth standards for Nigerian children. Ann Trop Paediatr 1981;1:27 - 37.
- [15] Arifeen SE, Black RE, Caufield LE, Antelman G, Baqui AH. Determinants of infant growth in the slums of Dhaka: size and maturity at birth, breast-feeding and morbidity. Eur J Clin Nutr 2001;55(3):167-78.
- [16] Chessex P. Nutritional problems and catch-up growth in infants with intrauterine growth retardation. In: Senterre J, editor. Intrauterine growth retardationNestle Nutrition Workshop Series, vol. 18 . New York: Nestle Ltd., Vevey/ Raren Press, Ltd., 1989.
- [17] Monset-Couchard M, de Bethmann O. Catch-up growth in 166 small-for-gestational age premature infants weighing less than 1000 g at birth. Biol Neonate 2000;78:161-7.
- [18] Verhoeff FH, Milligan P, Brabin BJ, Mlanga S, Nakoma V. Gestational age assessment by nurses in a developing country using the Ballard method, external criteria only. Ann Trop Paediatr 1977;17:333-42.
- [19] Brabin BJ. Fetal anaemia in malarious area: its causes and significance. Ann Trop Paediatr 1992;12:303-10.
- [20] Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KN, Mei Z, et al. CDC growth charts for the United States; methods and development. National Centre for Health Statistics. Vital Health Stat 2002;11(246).

- [21] Williams RL, Creasy RK, Cunningham GC, Hawes WE, Norris FD, Tashiro M. Fetal growth and perinatal viability in California. Obstet Gynecol 1982;59:624-32.
- [22] Labbe RF, Vreman HJ, Stevenson DK. Zinc protoporphyrin: a metabolite with a mission. Clin Chem 1999;45(12): 2060-72.
- [23] Letsky E. The haematological system. In: Hytten FE, Chamberlain G, editors. Clinical Physiology in Obstetrics. Oxford: Blackwell Science Ltd.; 1991. p. 2-75.
- [24] James WPT, Ferro-Luzzi A, Waterlow JC. Definition of chronic energy deficiency in adults. Eur J Clin Nutr 1988:42969-81.
- [25] World Health Organisation. Maternal anthropometry and pregnancy outcomes. Bull World Health Organ 1995;73:1-98 [Suppl.].
- [26] Cole TJ. The LMS method for constructing normalized growth standards. Eur J Clin Nutr 1990;44:45-60.
- [27] Verhoeff FH, Le Cessie S, Kalanda BF, Kazembe PN, Broadhead RL, Brabin BJ. Post-neonatal mortality in Malawi: the importance of maternal health. Ann Trop Paediatr 2004;24: 161-9.
- [28] Pelletier DL, Frongillo EA. Changes in child survival are strongly associated with changes in malnutrition in developing countries. Nutrition 2003;133:107-19.
- [29] Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet 2003;361(9376): 2226-34.
- [30] Rowland MGM, Cole TJ, Whitehead RG. A quantitative study into the role of infection in determining nutritional status in Gambian village children. Br J Nutr 1977;37:441-50.
- [31] Ashworth A, Morris SS, Lira PIC. Postnatal growth patterns in full-term low birth weight infants in Northeast Brazil are related to socioeconomic status. J Nutr 1997;127(2): 1950-6.
- [32] Kolsteren PW, Kusin JA, Kardjati S. Pattern of linear growth velocities of infants from birth to 12 months in Madura, Indonesia. Trop Med Int Health 1997;2(3):291-301.
- [33] Savage EJ. An evaluation of village based delivery of sulfadoxine-pyrimethamine for malaria control in pregnancy and the use of maternal anaemia and birthweight as indictors of malaria burden in pregnancy. PhD thesis, 2004 University of Liverpool.
- [34] Maleta K, Virtanen S, Espo M, Kulmala T, Ashorn P. Timing of growth faltering in rural Malawi. Arch Dis Child 2003;88(7): 574-8.
- [35] Arifeen S, Black RE, Caulfield LE, Antelman G, Baqui AH, Nahar Q, et al. Infant growth patterns in the slums of Dhaka in relation to birth weight, intrauterine growth retardation, and prematurity. Am J Clin Nutr 2000;72:1010-7.
- [36] De Onis Q, Yip Y. The WHO Chart: historical considerations and current scientific issues. In: Parrini M, Walter P, editors. Nutrition in pregnancy and growth. Bibl Nutr Dieta, vol. 53. Basel: Karger; 1996. p. 74-89.
- [37] Brabin BJ, Fletcher KA, Brown N. Do disturbances within the folate pathway contribute to low birthweight in malaria. Trends Parasitol 2003;19:39-43.
- [38] Menendez C. Malaria in pregnancy. Parasitol Today 1995;11: 178-83.
- [39] Le Cessie S, Verhoeff FH, Meningistie G, Kazembe P, Broadhead R, Brabin BJ. Changes in haemoglobin levels in infants in Malawi: effect of low birthweight and fetal anaemia. Arch Dis Child Neonatal Ed 2002;86:F182-7.
- [40] Brabin BJ, Kalanda BF, Verhoeff FH, Chimsuku LH, Broadhead RL. Risk factors for fetal anaemia in a malarious area of Malawi. Ann Trop Paediatr 2004;24:311-21.
- [41] Okoko BJ, Ota MO, Yamuah LK, Idiong D, Mkpanam SN, Avieka A, et al. Influence of placental malaria infection on

foetal outcome in the Gambia: twenty years after Ian McGregor. J Health Popul Nutr 2002;20(1):4-11.

- [42] Brabin BJ, Ramagosa C, Abdelgali S, Menendez C, Verhoeff FH, McGready R, et al. The sick placenta-the role of malaria. Placenta 2004;25:359-78.
- [43] Kalanda BF. Fetal and infant growth and nutrition in a malarious area of southern Malawi. PhD thesis, University of Liverpool; 2004.
- [44] Martorell R, Schroeder DG, Rivera JA, Kaplowitz HJ. Patterns of linear growth in rural Guatemalan adolescents and children. J Nutr 1995;125:1060S-7S.
- [45] Cole TJ. Relating growth rate to environmental factors methodological problems in the study of growth—infection interaction. Acta Paediatr Suppl 1989;350:14-20.
- [46] Leandro-Merhi VA, dos Santos-Vilela MM, da Silva MN, Lopez FA, de Azevedo-Barros-Filho A. Evolution of nutritional status of infants infected with the human immunodeficiency virus. Sao Paulo Med J/Rev Paul Med 2000; 118(5):148-53.
- [47] Cleland J, van Ginneken JK. Maternal education and child survival in developing countries: the search for pathways of influence. Soc Sci Med 1988;27:1357-68.