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Gestational weight gain and newborn anthropometric outcomes in rural Bangladesh

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Abstract
Low gestational weight gain (GWG) is a known predictor of fetal growth restriction in higher income countries, but there is little information on this association in lower income countries. Our objective is to describe the association between GWG and birth outcomes among pregnant women in rural Bangladesh. Pregnant women were identified in a community-based programme and enrolled into the study at an average of 13 weeks' gestation (n = 4,011). Maternal weight and height were measured at enrolment, maternal weight was measured at 36 weeks' gestation, and newborns were measured after birth. Rate of GWG (g/weeks) was calculated, and women were categorized as having adequate or inadequate GWG (Institute of Medicine recommendations). Newborn anthropometric outcomes included weight-for-age z score (WAZ), length-for-age z score (LAZ), head-circumference-for-age z score (HCZ), body mass index (BMI)-for-age z score (BMIZ), low birthweight (LBW < 2,500 g), WAZ < −2, LAZ < −2, HCZ < −2, BMIZ < −2, and small for gestational age (SGA: <10th percentile). Multivariate models were adjusted for confounders. Only 26% of the 2,562 women in these analyses had adequate GWG. Compared with newborns of women with inadequate GWG, infants of women with adequate GWG had a lower risk of adverse anthropometric outcomes (relative risk [95% confidence interval]: LBW = 0.68 [0.59, 0.80], LAZ < −2 = 0.64 [0.51, 0.80], HCZ < −2 = 0.75 [0.60, 0.93], BMIZ < −2 = 0.70 [0.59, 0.83], and SGA = 0.80 [0.73, 0.86]), but there was no significant difference in mean (*SE*) duration of gestation, 39.7 (0.08) versus 39.7 (0.05) weeks. In this population, GWG rate is a strong predictor of newborn anthropometric outcomes, but not duration of gestation.

KEYWORDS
body mass index, gestational age, gestational weight gain, low birthweight, small for gestational age, stunting

1 | INTRODUCTION

Fetal growth restriction is a major public health problem worldwide (Black et al., 2013) and particularly in Bangladesh (Christian et al., 2013; Islam et al., 2018; Khan, Islam, Awan, & Muurlink, 2018; Klemm et al., 2015; Mridha et al., 2016). Newborn anthropometric outcomes such as low birthweight (LBW), stunting at birth, and small for gestational age (SGA) are highly prevalent in low- and middle-income countries. In Bangladesh, the prevalence of LBW in 2012–2013 was 20% (Khan et al., 2018), prevalence of newborn stunting in various studies

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is of similar magnitude (Islam et al., 2018; Klemm et al., 2015 ; Mridha et al., 2016), and SGA is very common (e.g., 67.3% of infants born to mothers who received iron and folic acid during pregnancy, as stated in Klemm et al., 2015; Mridha et al., 2016). Birth length has been shown to be associated with compromised cognitive development (Lee et al., 2018), and LBW and restricted intrauterine growth have been linked with other longer term outcomes such as attained height, achieved schooling/education, and income later in life (Victora et al., 2008).

Gestational weight gain (GWG) is a well-known predictor of perinatal outcomes such as LBW (Goldstein et al., 2017; Han et al., 2011; Institute of Medicine [IOM] and National Research Council, 2009; McDonald et al., 2011). A systematic literature review followed by a meta-analysis of more than a million pregnancies, mainly in higher income countries (Goldstein et al., 2017), indicated that 23% of those women gained less weight than the 2009 IOM recommendations (IOM and National Research Council, 2009). Inadequate GWG was associated with 53% greater odds of SGA when compared with women with GWG within the IOM guidelines (Goldstein et al., 2017).

Very few studies have addressed the associations between GWG and birth outcomes in lower income countries (Gondwe et al., 2018; Ota et al., 2011), even though the prevalence of fetal growth restriction in such countries is much higher than in higher income countries (Black, Sacks, Xiang, & Lawrence, 2013). Thus, the aim of the analyses reported herein is to describe the associations between various GWG indicators and selected birth outcomes among women who participated in the Rang-Din Nutrition Study (RDNS) conducted in rural Bangladesh (Dewey et al., 2017; Matias et al., 2016; Mridha et al., 2016), and to explore whether these associations differ between adolescents (<20 years) and adult women, or between subgroups of women categorized by prepregnancy body mass index (BMI).

Key messages

- Few studies have addressed the associations between gestational weight gain and birth outcomes in lower income countries, even though the prevalence of fetal growth restriction in such countries is much higher than in higher income countries.
- Gestational weight gain rate was strongly and positively associated with newborn anthropometric status but was not associated with duration of gestation.
- The relative risk reductions for adverse birth outcomes among women with adequate gestational weight gain rate, compared with mothers with inadequate gestational weight gain rate, were 32% for low birthweight, 36% for newborn stunting, 25% for small newborn head size, 30% for newborn wasting, and 20% for small for gestational age.
- These results suggest that achieving adequate gestational weight gain could be an important step in reducing the burden of unfavourable birth outcomes in a low-income setting with high rates of maternal undernutrition.

2 | METHODS

2.1 | Study setting and population

The study was conducted in 11 unions of the Badarganj and Chirirbandar subdistricts in north-west Bangladesh. A union is the lowest administrative unit of the local government of Bangladesh. The study unions were located ~340 km from Dhaka in a rural region that was among the poorest in Bangladesh. In 2011, approximately half the population was living below the poverty line, about half of those over 7 years were illiterate, 75% had access to toilets or latrines, and 31% of households had electricity (Bangladesh Bureau of Statistics, 2011). Each union had three to four public health facilities as well as community-based health services provided by two non-governmental organizations (Mridha et al., 2016). The Lutheran Aid to Medicine in Bangladesh (LAMB) Community Health and Development Program provided the programmatic resources for conducting this trial and distributed the study interventions to participants. The University of California, Davis, and International Centre for Diarrhoeal Disease Research, Bangladesh, were responsible for evaluating the interventions.

2.2 | Study design, enrolment procedures, and data collection

The primary objective of the RDNS was to assess the impact of nutrient supplementation during the first 1,000 days on nutritional status of pregnant and lactating women and on growth, nutritional status, and development of their children. The study was a cluster-randomized effectiveness trial with four intervention groups, described in detail elsewhere (Mridha et al., 2016). During the prenatal period (the focus of these analyses), there were only two intervention groups: (a) control—pregnant women received one tablet of 60 mg of iron and 400 mg of folic acid daily during pregnancy (the standard of care), and (b) LNS—women received lipid-based nutrient supplements (20 g/day, 118 kcal) daily during pregnancy.

The RDNS was carried out in 64 clusters defined as the work area of a LAMB community health worker, each covering a population of 2,500–6,000. Sample size calculations were based on comparing the primary continuous outcomes between the four arms of the trial resulting in a minimum target sample size of 3,940 women, though 4,011 were ultimately enrolled as described elsewhere (Mridha et al., 2016).

LAMB identified potentially eligible pregnant women who were then contacted at home to obtain consent for screening. Eligibility criteria included gestational age of no more than 20 weeks. Gestational age was determined from the first day of the last menstrual period by maternal recall. Women were visited at home to collect baseline data on maternal and household characteristics and then asked to attend clinic visits where baseline anthropometric measurements were taken. Follow-up included a clinic visit at the 36th week of gestation to perform anthropometry and collect other information such as maternal morbidity. Birth visits were coordinated such that each woman would be visited by specially trained anthropometrists generally within 72 hr after birth. All anthropometrists were trained and standardized at the start of data collection and periodically afterwards using methods described by the World Health Organization (WHO; de Onis, Onyango, van den Broeck, Chumlea, & Martorell, 2004). At enrolment, maternal height was measured to the nearest 0.1 cm (ShorrBoard; Weigh and Measure LLC), and at each clinic visit, maternal weight was measured to the nearest 0.1 kg (Seca 874 Digital Floor Scale; Seca North America) and mid-upper arm circumference to the nearest 0.1 cm (ShorrTape; Weigh and Measure LLC). Newborn anthropometrists measured birthweight to the nearest 0.005 kg (DS4100 Infant Scale; Doran Scales Inc.), crown–heel length to the nearest 0.1 cm (ShorrBoard), and head circumference and mid-upper arm circumference to the nearest 0.1 cm (ShorrTape). Additional details on quality control and data collection have already been published (Mridha et al., 2016).

2.3 | Ethical approval

The study protocol was approved by the institutional review boards of the University of California, Davis; International Centre for Diarrhoeal Disease Research, Bangladesh; and LAMB. Participants provided written consent before data were collected. The study was registered at ClinicalTrials.gov (NCT01715038).

2.4 | Variable definitions

The birth outcomes assessed included crude weight (in g), length (in cm), head circumference (in cm), gestational age at the time of delivery (in weeks), weight-for-age *z* score (WAZ), length-for-age *z* score (LAZ), head-circumference-for-age *z* score (HCZ), and body mass index (BMI)-for-age *z* score (BMIZ). We defined LBW as a birthweight < 2,500 g, newborn wasting as WAZ < −2, newborn stunting as LAZ < −2, small head size as HCZ < −2, and low BMIZ as BMIZ < −2 (a measure of body proportionality). The WHO 2006 Child Growth Standards were used to determine *z* scores for birthweight, length, head circumference, and BMI (WHO, 2006). SGA was defined as birthweight below the INTERGROWTH 10th percentile for infants of the same gestational age and sex (Villar et al., 2014). In this study, 86% of anthropometric measurements took place within 2 days of birth and 98% within 14 days. Mean age of the newborns on the day of measurement was 2.04 ± 2.75 days. Infants measured after 14 days of birth were excluded from analysis. Infants measured between 3 and 14 days of birth had their birth measurements back calculated assuming that the respective *z* score remained constant (Mridha et al., 2016).

GWG was defined in several different ways: (a) total GWG from enrolment to 36 weeks calculated as the difference between the weight at 36 weeks' gestational and the weight at the first pregnancy assessment (between 9 and 16 weeks); (b) GWG rate (g/week) calculated as the total GWG divided by the duration of the interval between assessments; (c) GWG rate adequacy (a dichotomous variable), based on the IOM recommendations (GWG rate adequacy), determined by considering the rate of weight gain appropriate for the estimated prepregnancy BMI; (d) GWG *z* score according to the INTERGROWTH 21st century standard, based on the total GWG for gestational age at the 36 weeks' gestation assessment (calculated only for those women with prepregnancy BMI between 18.5 and 24.9 kg/m^2, a criterion imposed by the INTERGROWTH study; Cheikh-Ismail et al., 2016); (e) INTERGROWTH GWG *z* score at 36 weeks below −2 (a dichotomous variable). We used these five different ways of expressing GWG for the descriptive aspects of the study, and we selected two of those variables (GWG rate and GWG rate adequacy) as the key predictors to be examined with respect to birth outcomes because they are least influenced by the total duration of gestation and allow for use of the full sample size (i.e., they are not constrained by the availability of information in the INTERGROWTH 21st study, which excluded underweight and overweight women).

The IOM guidelines stipulate that women should gain weight according to their prepregnancy BMI—that is, those who were underweight (BMI < 18.5 kg/m^2), normal weight (BMI = 18.5–24.9 kg/m^2), overweight (BMI = 25.0–29.9 kg/m^2), or obese (BMI $\geq$ 30.0 kg/m^2) should gain between 12.5 and 18.0, between 11.5 and 16.0, between 7.0 and 11.5, and about 7.0 kg, respectively. We defined insufficient GWG as a value below the appropriate interval for each woman, excessive GWG as a value above the appropriate interval, and normal GWG as a value within the appropriate interval. For the purpose of the current analyses, we dichotomized this variable as adequate (combined normal and excessive GWG) and inadequate (insufficient GWG) because the number of women who were overweight prior to pregnancy was very small. Because the initial anthropometric measurements were taken during early pregnancy, prepregnancy BMI was estimated by extrapolating back to conception using linear regression, after first establishing that the relationship between BMI and gestational age at enrolment was linear in our sample (Mridha et al., 2016). We then extrapolated to the first day of gestation by multiplying the gestational age at enrolment by the coefficient for BMI by gestational age and by subtracting that value from enrolment BMI. We used principal components analysis to construct a socio-economic index on the basis of a set of 27 questions about land and asset ownership, as well as housing and sanitation quality. The Household Food Insecurity Access Scale was used to construct a food insecurity score and categories (Coates, Swindale, & Bilinsky, 2007).

2.5 | Statistical analysis and sample size

The available sample size was sufficient to detect a correlation of at least .065 assuming a type I error rate of 5%, 80% power, and an intracluster correlation of .01 in the full sample. We were powered to detect a correlation of ≥.10 within the adolescent subset and ≥.08 within the adult women. Primary analyses were performed using R Version 3.4.0 (R Foundation for Statistical Computing, Austria, 2017). All analyses controlled for the cluster-randomized design by including cluster as a random effect with regional union and intervention group as additional control covariates, even though there was no significant main effect of intervention group on GWG (Matias et al., 2016). We used cluster-adjusted chi-square tests to describe differences in maternal characteristics for variables with more than two categories each and linear models for testing mean differences between groups. Models were constructed for testing the association with GWG variables using linear regression for continuous outcomes and modified Poisson regression for dichotomous outcomes. These associations were first assessed in unadjusted models and then tested in multivariate models adjusting for covariates including maternal prepregnancy BMI, height, age, gestational age at enrolment, years since menarche, nulliparity, education, socio-economic status, season at birth, and household food insecurity. We also performed sensitivity analyses excluding those mothers with excessive GWG from the adequate GWG category.

In separate models, we assessed whether selected characteristics modified the associations between GWG variables and the outcomes, by adding an interaction term. Due to model convergence problems, mixed logistic regression was used to assess interactions for dichotomous outcomes. Significant interactions ($P < .05$) were further examined with stratified analyses and estimation of separate regression lines to better understand the nature of the interaction. The characteristics tested for interactions were nulliparity (nulliparous vs. parous), maternal prepregnancy BMI (low BMI < 18.5 kg/m^2 vs. BMI ≥ 18.5 kg/m^2), education (primary or less vs. any secondary), socio-economic status (by socio-economic index tertiles), age (adolescents vs. adults – 20 years +), height (height < 150 cm for adults and <−2 *SD* for adolescents, vs. taller), and food insecurity (any insecurity vs. food secure).

3 | RESULTS

The RDNS enrolled 4,011 pregnant women of whom 2,562 had adequate data for these analyses (credible gestational ages at delivery and anthropometric data available for the mother at enrolment and 36 weeks' gestation and for the infant at birth). Gestational ages were not considered credible if delivery took place outside of 28–44 weeks or was associated with birthweights that were >3.5 *SD* units outside of reference data generated in the local setting (Mridha et al., 2016). The primary reason for loss to follow-up for these analyses was lack of data at 36 weeks' gestation due to pregnancy loss, live birth before 36 weeks, or non-attendance at the 36th-week clinic visit (Figure 1). Compared with women who were included (n = 2,562) in the analytical sample, those who were not included because of ineligibility or lack of maternal or infant anthropometric data (n = 1,449) were, on average, slightly older (22.2 vs. 21.9 years; P = .036), were less educated (5.9 vs. 6.4; P < .001), and had a lower asset index (−0.15 vs. 0.09; P = .014) and their newborns had lower birth anthropometric outcomes (P < .001; Table S1).

At enrolment, 35% of the women were underweight and 5% were overweight. Mean (*SD*) gestational age at enrolment was 13 (3.4) weeks, and the women were 21.9 (4.9) years of age. Adolescents accounted for 40% of the sample. Food insecurity prevalence was 52% (Table 1). The overall values for GWG, GWG rate, and GWG rate adequacy were 6.51 kg, 297 g/week, and 26%, respectively. Total GWG and GWG rates were significantly higher among adolescents compared with adults, but GWG rate adequacy did not differ by maternal age category.

Figure 2 shows the percentage of women with insufficient, normal, and excessive IOM GWG rate, which varied significantly according to prepregnancy BMI. The percentage with insufficient IOM GWG rate was very high (87%) among those with low prepregnancy BMI, 70% among those with normal prepregnancy BMI, and 34% among those who were overweight prior to pregnancy. The proportion of women who gained weight within the IOM guidelines was similar between women with normal versus overweight prepregnancy BMI (25% vs. 23.8%, P = .831), but the proportion with excessive IOM GWG rate was higher among overweight women than among underweight or normal-weight women (42.1% vs. 5% and 2.1%, respectively).

GWG rate was strongly associated with all infant anthropometric outcomes at birth, but not with gestational age at delivery (Table 2). For every 100 g/week of increase in GWG rate, birthweight increased by +74.5 g, birth length increased by +0.28 cm, and WHO WAZ increased by +0.18. Similarly, for every 100 g/week of increase in GWG rate, there was a reduction in risk of 20% for LBW, 22% for newborn stunting, 19% for small head size, 18% for newborn wasting, and 11% for SGA. The results were the same in unadjusted (data not shown) and adjusted models, implying that there was little confounding by covariates.

When comparing outcomes between women with IOM adequate versus inadequate GWG rates, there were highly significant differences in all of the continuous newborn anthropometric outcomes (e.g., +128.1 g of birthweight, +0.25 LAZ, +0.25 HCZ, and +0.29 BMIZ), but no difference in gestational age at delivery (Table 3).

Overall, 36% of infants had LBW, 18% were stunted, 21% had small head size, 32% were wasted (low WHO BMIZ), and 65% were SGA. LBW, low LAZ, small head size, wasting, and SGA were less likely among infants of women with GWG rate adequacy, compared with those with inadequate GWG rate (Figure 3; relative risks and 95% confidence intervals were 0.68 [0.59, 0.80], 0.64 [0.51, 0.80], 0.75 [0.60, 0.93], 0.70 [0.59, 0.83], and 0.80 [0.73, 0.86], respectively. Results were similar when excluding mothers with excessive GWG rate (data not shown).

The associations between GWG and birth outcomes were modified by four of the seven potential effect modifiers examined, specifically low prepregnancy BMI, nulliparity, education, and socio-economic status (P for interactions < .05). The relationship between newborn LAZ and GWG rate was steeper among mothers with low prepregnancy BMI, so that average LAZ among their newborns was similar to that of newborns born to women with normal prepregnancy

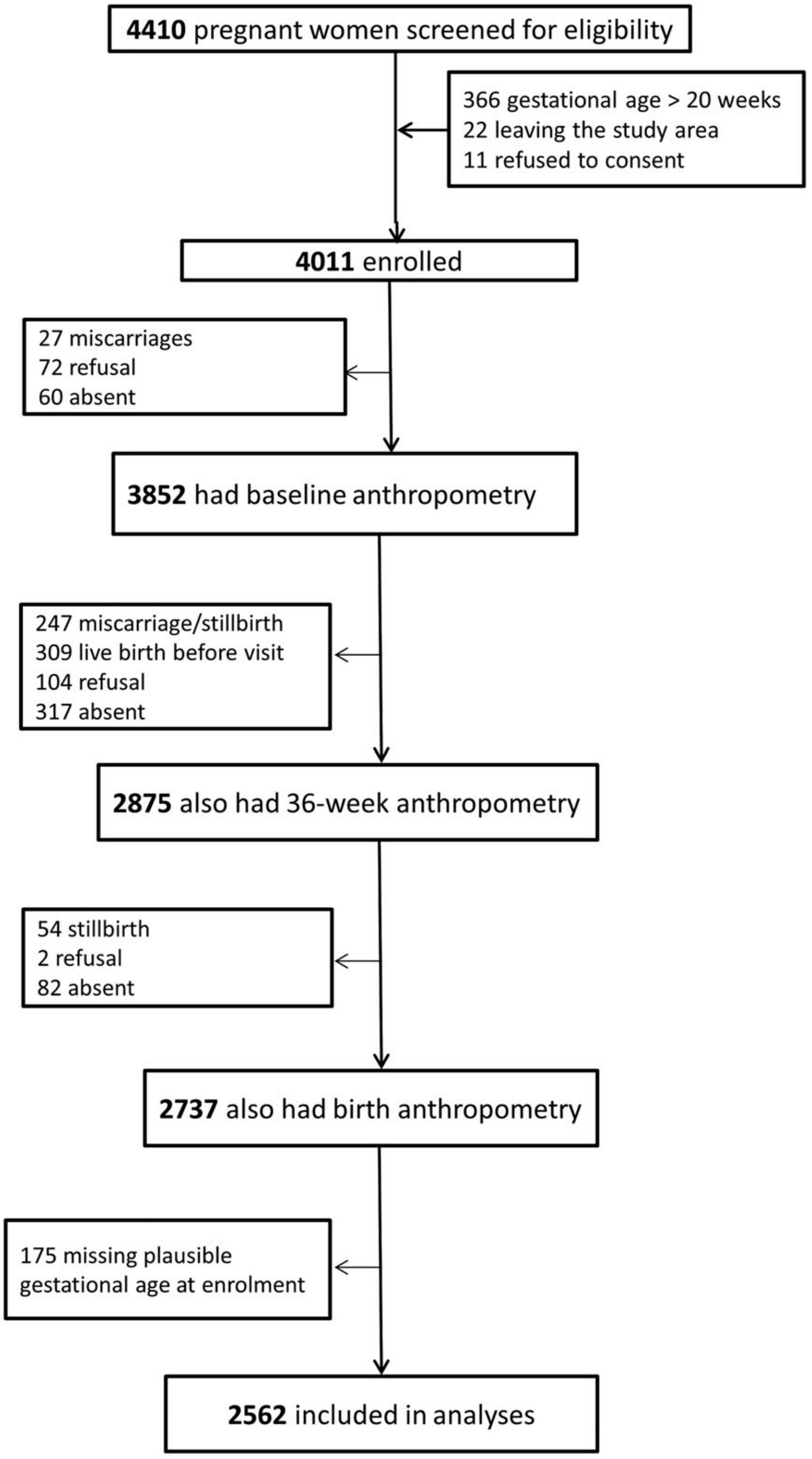

FIGURE 1 Flow chart of study participants in the Rang-Din Nutrition Study. For twin births, numbers include one randomly selected twin from each twin pair

BMI if GWG was >500 g/week (Figure 4). Among nulliparous women, average newborn LAZ among those who had adequate GWG was much higher than that among those with inadequate GWG and very similar to average LAZ of newborns born to parous women (Figure 5). This pattern was similar for birth length (data not shown). With regard to education and socio-economic status, the relationship between GWG rate and birthweight, WAZ, BMIZ, and SGA was stronger among mothers who were wealthier or had more education, than among mothers who were poorer or had less education (data not shown).

4 | DISCUSSION

In this study population, mean GWG from enrolment to 36 weeks' gestation was only 6.5 kg, and 74% of the pregnant women had an

TABLE 1 Maternal gestational weight gain and enrolment characteristics[a]

Characteristics	N	All	n	Adults	n	Adolescents
Prepregnancy BMI, kg/m^2	2,560	19.8 ± 2.7	1,562	20.2 ± 2.9	998	19.1 ± 2.2
Height, cm	2,562	150.7 ± 5.4	1,563	150.8 ± 5.3	999	150.5 ± 5.4
Gestational age at enrolment, weeks	2,562	13.0 ± 3.4	1,563	13.0 ± 3.4	999	12.9 ± 3.3
Age, years	2,562	21.9 ± 4.9	1,563	24.7 ± 4.2	999	17.4 ± 1.3
Years since menarche	2,562	9.3 ± 4.9	1,563	12.1 ± 4.2	999	5.0 ± 1.6
Maternal education, years of study	2,562	6.4 ± 3.2	1,563	6.2 ± 3.5	999	6.7 ± 2.6
Asset index	2,562	0.09 ± 2.2	1,563	0.06 ± 2.3	999	0.13 ± 2.0
Food insecure[b]	2,562	52%	1,563	55%	999	47%
GWG from enrolment to 36 weeks, kg[c]	2,561	6.51 ± 2.75	1,563	$6.37 \pm 2.74_a$	998	$6.73 \pm 2.76_b$
GWG rate, g/week[c]	2,561	297 ± 126	1,563	$292 \pm 127_a$	998	$305 \pm 125_b$
GWG rate adequacy	2,559	26%	1,562	26%	997	25%
INTERGROWTH GWG z at 36 weeks[d]	1,178	−1.46 ± 1.01	742	−1.49 ± 1.01	436	−1.41 ± 1
INTERGROWTH GWG $z < -2$ at 36 weeks[e]	1,178	27%	742	28%	436	26%

Note. Prepregnancy BMI was back calculated by extrapolating the relationship between gestational age and BMI at enrolment within the sample.

Abbreviations: BMI, body mass index; GWG, gestational weight gain; IOM, Institute of Medicine.

[a]Values are means ± *SD*s or %. Adolescents are 19 years or younger. Adults are 20 years or older.

[b]Any level of food insecurity by the Household Food Insecurity Access Scale (Coates et al., 2007).

[c]Letters in subscript indicate statistical testing between adults and adolescents, with significance indicated by differing letters. GWG $P = .001$; GWG rate $P = .011$.

[d]Institute of Medicine weight gain recommendations for pregnancy (Institute of Medicine (United States) and National Research Council (States) Committee to Reexamine IOM Pregnancy Weight Guidelines—IOM, 2009).

[e]INTERGROWTH 21st century standard values at 36 weeks' gestation (Cheikh-Ismail et al., 2016).

inadequate GWG rate according to IOM guidelines. GWG rate was strongly and positively associated with child anthropometric status at birth but was not associated with gestational age at delivery. The relative risk reductions for adverse birth outcomes among women with adequate GWG rate, compared with mothers with inadequate GWG rate, were 32% for LBW, 36% for newborn stunting, 25% for small newborn head size, 30% for newborn wasting, and 20% for SGA.

If these associations are causal, they suggest that achieving adequate GWG could be an important step in reducing the burden of unfavourable birth outcomes in a low-income setting with high rates of maternal undernutrition. We found only two other studies in lower income countries that addressed the association between GWG and birth outcomes (Gondwe et al., 2018; Ota et al., 2011). In rural Malawi, women with low weekly weight gain were at increased risk of having infants with LBW and small head circumference ($P = .024$) than were those with normal weight gain (Gondwe et al., 2018). In Vietnam, GWG < 10 kg was associated with 90% greater odds of SGA than was GWG of 10–15 kg (Ota et al., 2011). Previous studies relating GWG and birth outcomes have been conducted in middle- and high-income countries and have generally investigated LBW, SGA, and large for gestational age as outcomes. The risk reduction in LBW associated with adequate GWG in our study population (32%) was smaller than the estimates from studies in Japan (42%, Tsukamoto et al., 2007) and the United States (44%, Helms, Coulson, & Galvin, 2006; and 50%, Frederick, Williams, Sales, Martin, & Killien, 2008). Similarly, the risk reduction in SGA associated with adequate GWG in our study population (20%) was smaller than were estimates for women in a meta-analysis (35%, Goldstein et al., 2017). The smaller risk reductions we observed may be partially explained by differences in partitioning of nutrients between the mother and fetus. In low-income countries such as Bangladesh, maternal undernutrition may trigger greater use of energy and nutrients to sustain the mother's nutritional status, as well as to fight infections, with the result being that less is available for fetal growth (King, 2003).

Only a few studies have examined the relationship between GWG and other anthropometric birth outcomes such as LAZ (Dahly et al., 2018; Diesel et al., 2015), HCZ (Wander et al., 2015), and BMIZ (Diesel et al., 2015). In Ireland, birth length did not differ significantly between infants of mothers with excessive GWG and those of mothers with inadequate or healthy GWG (Dahly et al., 2018). In the United States, there were no significant differences in LAZ at birth when women with inadequate and adequate GWG were compared (Diesel et al., 2015). These results are in contrast with our findings showing that GWG was strongly related to birth length and LAZ and with those results reported by Gondwe et al. (2018) showing that average weekly weight gain was positively associated with birthweight and LAZ. However, in another U.S. study of 3,601 women (Wander et al., 2015), a 1-kg increase in total GWG was associated with a +0.04-cm difference in HC, a value that it is virtually identical to the one observed in our cohort. Gondwe et al. also found that average

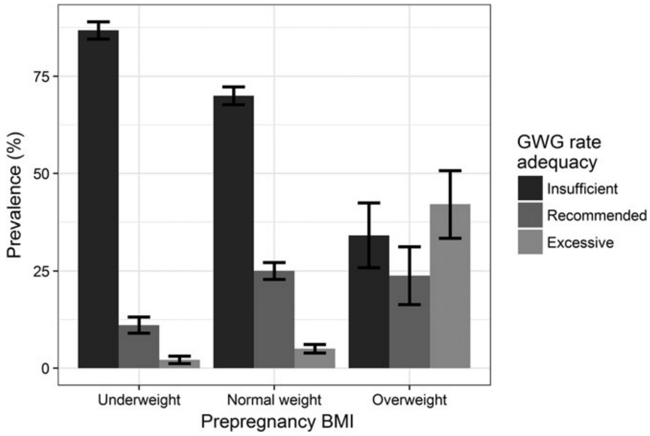

FIGURE 2 Gestational weight gain (GWG) rate adequacy stratified by prepregnancy body mass index (BMI). The panel represents the proportion of women with GWG classified on the basis of the Institute of Medicine and the prepregnancy BMI. There were 894 underweight women of whom 86.8% (n = 776) had an insufficient GWG rate, 11.1% (n = 99) had the recommended GWG rate, and 2.1% (n = 19) had an excessive GWG rate. There were 1,539 normal women of whom 70.0% (n = 1,077) had an insufficient GWG rate, 25.0% (n = 385) had the recommended GWG rate, and 5.0% (n = 77) had an excessive GWG rate. There were 126 overweight women of whom 34.1% (n = 43) had an insufficient GWG rate, 23.8% (n = 30) had the recommended GWG rate, and 42.1% (n = 53) had an excessive GWG rate. Type of GWG significantly differed by prepregnancy BMI category by chi-square test (P < .001). Underweight: prepregnancy BMI <18.5 kg/m^2. Normal weight: prepregnancy BMI = 18.5–24.9 kg/m^2. Overweight: prepregnancy BMI ≥ 25.0 kg/m^2

TABLE 2 Associations between gestational weight gain rate and birth outcomes (n = 2,559)[a]

	Gestational weight gain rate (100 g/week)	
Outcomes	**β coefficient [95% CI]**	**P[b]**
Birthweight, g	74.50 [63.17, 85.83]	<.0001
Birth length, cm	0.28 [0.22, 0.34]	<.0001
Head circumference, cm	0.19 [0.15, 0.23]	<.0001
Gestational age, weeks	−0.04 [−0.1, 0.02]	.183
WAZ	0.18 [0.15, 0.20]	<.0001
LAZ	0.14 [0.11, 0.17]	<.0001
HCZ	0.15 [0.12, 0.18]	<.0001
BMIZ	0.17 [0.14, 0.20]	<.0001
	Relative risk [95% CI]	P[b]
Low birthweight	0.80 [0.75, 0.85]	<.0001
Low[a] WAZ	0.79 [0.74, 0.85]	<.0001
Low LAZ	0.78 [0.72, 0.85]	<.0001
Low HCZ	0.81 [0.75, 0.87]	<.0001
Low BMIZ	0.82 [0.77, 0.88]	<.0001
Small for gestational age	0.89 [0.85, 0.93]	<.0001

Abbreviations: BMI, body mass index; BMIZ, BMI-for-age z score; HCZ, head-circumference-for-age z score; LAZ, length-for-age z score; WAZ, weight-for-age z score.

[a]Low defined as z score < −2 SD. Low birthweight defined as below 2,500 g. Small for gestational age defined as below INTERGROWTH 10th percentile for children of the same gestational age and sex.

[b]Parameter estimates and P derived from linear or modified Poisson mixed regression adjusted for prepregnancy BMI, maternal height, gestational age at enrolment, age, years since menarche, education, socio-economic status, food security, nulliparity, and season of birth and controlling for the cluster randomization and treatment assignment of the trial. Intracluster correlation was zero for the primary outcomes.

weekly weight gain was positively associated with HC. With regard to BMIZ, Diesel et al. (2015) reported that newborns of women with inadequate GWG had lower BMIZ at birth (−0.44 z-score units) than newborns of women with adequate GWG, a difference that was considerably greater than the difference observed in our cohort (−0.17 z score units).

The associations between GWG and birth outcomes were modified by some maternal characteristics such as low prepregnancy BMI, nulliparity, education, and socio-economic status, but not by age category, short stature, or food insecurity. Our a priori hypothesis was that the association between GWG and the birth outcomes would differ according to maternal age category, that is, between adolescents and adults, but we did not find a significant interaction with maternal age. This implies that the potential benefits of adequate GWG, with regard to infant birth size, did not differ between adults and adolescents even though adolescents are at higher risk for adverse birth outcomes (Das et al., 2017). The relationships of GWG rate with birth outcomes were stronger among women who had low prepregnancy BMI or were nulliparous. Those subgroups may have more potential to benefit from improved GWG. In a recent systematic literature review followed by a meta-analysis, the pooled odds ratio for the association between insufficient GWG and SGA was 1.53, based on 11 studies, but was 1.89 among women with low prepregnancy BMI, based on nine studies (Goldstein et al., 2017), suggesting a stronger relationship of GWG to SGA among women with low BMI. In another systematic literature review followed by a meta-analysis with emphasis on ethnicity, the risk of SGA and LBW remained elevated for those women with GWG below the IOM guideline when regional cut-off points were used to classify prepregnancy BMI in East Asia instead of the traditional WHO cut-off points (Goldstein et al., 2018).

In the RDNS, GWG rate was not associated with gestational age at delivery. This is consistent with findings from the United States, Ireland, and Taiwan (Dahly et al., 2018; Huang et al., 2018; Sharma et al., 2015), but not with several other reports suggesting that low GWG is associated with prematurity (Black, Sacks, et al., 2013; Enomoto et al., 2016; Li et al., 2013; Shin & Song, 2015) or duration of gestation (Gondwe et al., 2018). One potential explanation for these conflicting results is that most of the studies that have shown an association failed to adjust total GWG for gestational age at last measurement or otherwise account for the duration of pregnancy by calculating GWG rate (Sharma et al., 2015). Women who deliver early have less time to gain weight, so the relationship between total GWG and preterm birth could be due to reverse causation.

TABLE 3 Associations between gestational weight gain rate adequacy and continuous birth outcomes (n = 2,559)[a]

Outcomes	Gestational weight gain rate adequacy Yes (26%) Mean ± *SE*	 No (74%) Mean ± *SE*	 Difference in means [95% CI]	*P*
Birthweight, g	2,714 ± 15.0	2,586 ± 10.1	128.1 [95.1, 161.0]	<.0001
Birth length, cm	47.9 ± 0.08	47.4 ± 0.05	0.50 [0.33, 0.67]	<.0001
Head circumference, cm	33.0 ± 0.05	32.7 ± 0.03	0.32 [0.21, 0.43]	<.0001
Gestational age, weeks	39.7 ± 0.08	39.7 ± 0.05	−0.07 [−0.24, 0.10]	.426
WAZ	−1.28 ± 0.04	−1.58 ± 0.02	0.30 [0.22, 0.38]	<.0001
LAZ	−0.97 ± 0.04	−1.22 ± 0.03	0.25 [0.16, 0.34]	<.0001
HCZ	−1.04 ± 0.04	−1.29 ± 0.03	0.25 [0.16, 0.33]	<.0001
BMIZ	−1.10 ± 0.05	−1.46 ± 0.09	0.29 [0.20, 0.37]	<.0001

Abbreviations: BMI, body mass index; BMIZ, BMI-for-age *z* score; HCZ, head-circumference-for-age *z* score; LAZ, length-for-age *z* score; WAZ, weight-for-age *z* score.

[a]Mean and difference in means estimates are adjusted for prepregnancy BMI, maternal height, gestational age at enrolment, age, years since menarche, education, socio-economic status, food security, nulliparity, and season of birth and controlling for the cluster randomization and treatment assignment of the trial. Intracluster correlation was zero for the primary outcomes.

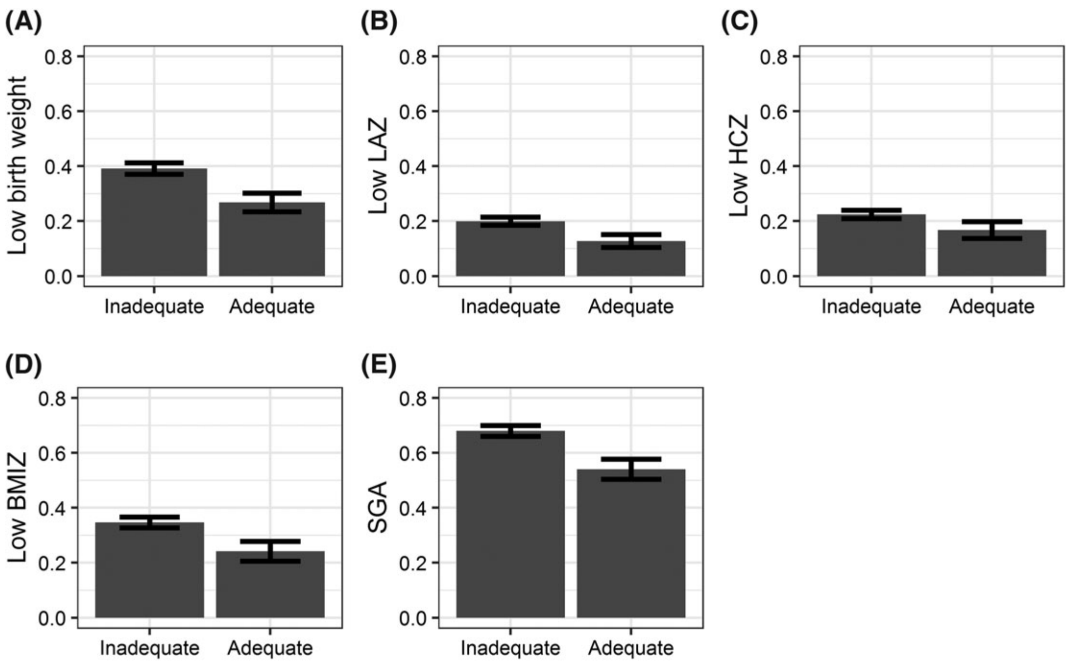

FIGURE 3 Prevalence of low birthweight (a), low LAZ (b), low HCZ (c), low BMIZ (d), and SGA (e) dichotomous outcomes by gestational weight gain rate adequacy based on Institute of Medicine (IOM) guidelines. Each panel shows prevalence and 95% CI within IOM gestational weight gain status: inadequate or adequate (normal or excessive) gestational weight gain rate groups. Low *z* score is defined as <−2. In each panel, the prevalence of adverse birth outcomes is lower in the adequate IOM gestational weight gain rate group with reduced risks of (a) low birthweight (birthweight < 2,500 g), 0.68 [0.59, 0.80]; (b) low length-for-age *z* score (LAZ), 0.64 [0.51, 0.80]; (c) low head-circumference-for-age *z* score (HCZ), 0.75 [0.60, 0.93]; (d) low body-mass-index-for-age *z* score (BMIZ), 0.70 [0.59, 0.93]; and (e) small for gestational age (SGA), 0.80 [0.73, 0.86] based on a sample size of 2,559

The present study has several limitations. First, the assessment of maternal BMI could not be performed earlier than the 13th gestational week for approximately half of the study sample, which may have resulted in misclassification of prepregnancy BMI status. However, this misclassification should have been the same for all prepregnancy BMI groups. Second, the analytic sample was slightly younger, had more education, and had a higher socio-economic index than those excluded, which could restrict the generalizability of our findings to the original target population. Moreover, because it was impossible to calculate GWG rate for women who delivered before 36 weeks, when the second weight measurement was taken, the analytical sample includes fewer women who delivered preterm than the original

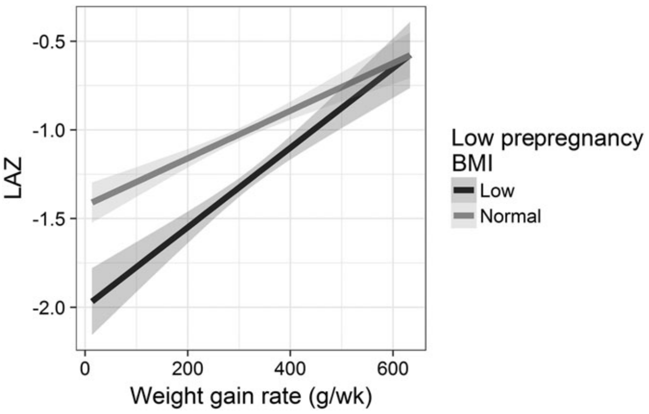

FIGURE 4 Relationship between gestational weight gain and newborn length-for-age *z* score (LAZ) stratified by prepregnancy body mass index (BMI). Panel shows the association between LAZ and rate of gestational weight gain stratified by prepregnancy BMI. *P* for interaction = .046. The light grey line indicates low BMI, and the dark line shows normal or overweight BMI. The bands are 95% confidence intervals from mixed model linear regression. Underweight: prepregnancy BMI < 18.5 kg/m^2. Normal weight: prepregnancy BMI = 18.5–24.9 kg/m^2. Overweight: prepregnancy BMI ≥ 25.0 kg/m^2

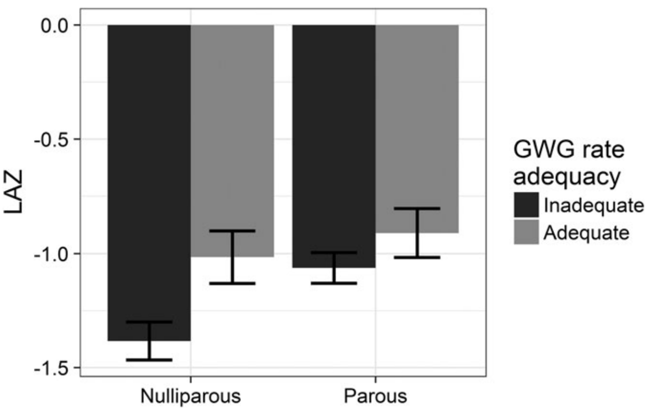

FIGURE 5 Relationship between gestational weight gain and newborn length-for-age *z* score (LAZ) stratified by parity. Panel shows mean and 95% CI for LAZ in gestational weight gain (GWG) rate adequacy groups stratified by maternal parity. *P* for interaction = 0.011. Institute of Medicine (IOM) adequate GWG (combined normal and excessive GWG) and inadequate GWG (insufficient GWG). IOM guidelines recommend GWG according to prepregnancy BMI: Underweight, normal-weight, overweight, or obese women should gain between 12.5 and 18.0, between 11.5 and 16.0, between 7.0 and 11.5, and about 7.0 kg, respectively. We categorized values below these intervals as insufficient GWG, above as excessive, and within as normal GWG

target population, which may limit our ability to detect an association between GWG and duration of gestation. Strengths of the study include a relatively large sample size, a low attrition rate, anthropometric data collection conducted by a well-trained and standardized team, the use of several variables to express GWG, and inclusion of several different birth outcomes. Finally, it is noteworthy that the unadjusted and adjusted models yielded very similar results, implying that confounding was minimal, although there is still the possibility that unmeasured confounders could have biased the findings.

In conclusion, these results suggest that in this low-income cohort, GWG is a strong predictor of anthropometric birth outcomes, but not duration of gestation. The association between GWG and birth outcomes was modified by prepregnancy BMI and parity. These results reinforce the importance of starting pregnancy with a healthy body weight and keeping GWG within the recommended guidelines. In lower income countries such as Bangladesh where total GWG is low and insufficient GWG is highly prevalent, research is needed to evaluate whether encouraging and promoting adequate GWG could reduce the burden of unfavourable birth outcomes. Such interventions could provide counselling regarding appropriate weight gain, nutrition, health care, and hygiene practices and may need to be coupled with control of infections during pregnancy (Jahan et al., 2014), as well as behavioural self-monitoring and rewards for successful behaviour (Hill, Skouteris, & Fuller-Tyszkiewicz, 2013).

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

The authors' responsibility were as follows: SLM, MKM, and KGD designed the research; MKM conducted the research; CDA performed the statistical analysis; GK wrote the first draft of the manuscript and had primary responsibility for final content; KGD was the principal investigator for the overall project; and all authors read and approved the final manuscript.

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