



Effectiveness of wheat soya blend supplementation during pregnancy and lactation on pregnancy outcomes and nutritional status of their infants at 6 months of age in Thatta and Sujawal districts of Sindh, Pakistan: a cluster randomized-controlled trial

Gul Nawaz Khan¹ · Shabina Ariff¹ · Sumra Kureishy² · Muhammad Sajid¹ · Arjumand Rizvi¹ · Cecilia Garzon² · Mica Jenkins³ · Saskia de Pee^{3,4,5} · Sajid Bashir Soofi¹ · Zulfiqar A. Bhutta⁶

Received: 14 June 2019 / Accepted: 11 May 2020 / Published online: 24 May 2020
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

Abstract

Purpose We aimed to assess the effectiveness of wheat soya blend plus (WSBP) provided during pregnancy and lactation on weight gain during pregnancy, reduction of low birthweight (LBW), and improvement in nutritional status in infants at 6 months of age in Thatta and Sujawal districts of Sindh, Pakistan.

Methods A cluster randomized-controlled trial was conducted in Thatta and Sujawal districts in Pakistan from August 2014 to December 2016. A total of 2030 pregnant women were enrolled in the study. These women and their infants were followed during pregnancy and first 6 months of life. Pregnant women received a monthly ration of 5 kg (i.e., 165 g/day) of WSB + during pregnancy and the first 6 months of their lactation period.

Results There was no difference in weight gain during pregnancy between the intervention and control groups ($n = 496$, 326.7 g/week 95% CI 315.2–338.1 vs. ($n = 507$, 306.9 g/week, 95% CI 279.9–333.9 $P = 0.192$), after adjustment with different factors. The reduction in the prevalence of LBW was not different between intervention and control groups ($n = 325$, 34.0%, 95% CI 31.7–36.4, vs. ($n = 127$, 34.3%, 95% CI 27.2–41.5, $P = 0.932$). Significant reductions in risk of stunting ($n = 1319$ RR 0.85, 95% CI 0.73–0.99, $P = 0.041$), wasting ($n = 1330$ RR 0.77, 95% CI 0.65–0.91, $P = 0.003$), and underweight ($n = 1295$ RR 0.77, 95% CI 0.69–0.87, $P < 0.001$) were observed in infants at 6 months of age in the intervention as compared to the control group. However, no difference was noted on reduction in the risk of stunting among infants at 6 months of age in the intervention and control group ($n = 1318$ RR 0.91, 95% CI 0.78–1.07, $P = 0.253$) after adjustment. A significant reduction in anemia was noted ($n = 1328$ RR 0.94, 95% CI 0.91–0.98, $P = 0.002$) in infants at 6 months of age in the intervention as compared to the control group in adjusted analysis.

Conclusions Provision of WSB + during pregnancy and the first 6 months of lactation is effective in reducing the risk of under nutrition and anemia in infants at 6 months of age. This study can potentially guide the government and donor agencies in investing in nutritional programmes, especially for pregnant and lactating women living in vulnerable settings.

Keywords Wheat soya blend · Weight gain · Low birthweight · Stunting · Wasting

Abbreviations

AKU Aga Khan University
LHW Lady health worker

LNS Lipid-based nutrient supplements
MICS Multiple indicator cluster survey
MNP Micro-nutrient powders

✉ Sajid Bashir Soofi
sajid.soofi@aku.edu

¹ Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan

² World Food Programme, Islamabad, Pakistan

³ World Food Programme, Rome, Italy

⁴ Friedman School of Nutrition Science and Policy, Tufts University, Boston, MA, USA

⁵ Division of Human Nutrition, Wageningen University, Wageningen, Netherlands

⁶ Institute for Global Health and Development, A, Aga Khan University, Karachi, Pakistan

PLW Pregnant and lactating women
 UC Union council
 WSBP Wheat soya blend plus

Introduction

For healthy pregnancy and birth outcomes, it is essential that women have adequate nutritional status during preconception, pregnancy, and postpartum [1–3]. In developing countries, such as Pakistan, women experience multiple biological and social stressors including food insecurity, poor health care, inadequate diets, recurrent infections, gender inequalities, heavy work burdens, repeated pregnancies, and short intervals between pregnancies. These stressors increase their risk of malnutrition, including low BMI, anemia, and micronutrient deficiencies (vitamin A, calcium, zinc, folate, iodine, iron, and vitamin D) among women [4–6].

Maternal malnutrition (often indicated by low BMI or low MUAC) is associated with increased rates of infections, obstructed labour, and small-for-gestational-age (SGA) babies. The process of a child becoming stunted often begins in the womb or soon after birth and may continue until 2 years of age [7, 8]. Stunting is a consequence of inadequate nutrition, often combined with frequent infection, which also leads to increased risk of death and disease, impaired cognitive development, reduced educational achievements, reduced work productivity, and lower earnings [9–14].

Evidence from low- and middle-income countries demonstrates that the provision of nutrition-based supplementation during pregnancy and lactation is safe, and can improve foetal growth, reduce perinatal mortality, decrease prevalence of low birthweight (LBW), and SGA babies [15–21], and lower the risk of stunting among children under 24 months of age [10, 22–24]. Balanced energy-protein supplements referred to as nutrition-based supplements contain less than 25% protein as their total energy content. According to the WHO recommendations on antenatal care for a positive pregnancy experience, these supplements are intended for populations or areas with a high prevalence ($\geq 20\%$) of pregnant women who are undernourished or at risk of becoming undernourished, and promote gestational weight gain and improve birth outcomes [25]. Globally, maternal supplementation with balanced energy-protein supplements have shown a 34% reduction in the risk of SGA and stillbirths [23, 26]. Moreover, research has demonstrated a 32% reduction in the risk of LBW [27]. In terms of children provided with nutrition-based supplements, regardless of nutrition counselling, were shown to improve weight gain, and height gain among children under 2 years of age. Another study found that the provision of nutrition-based supplements reduced stunting for children under 2 years of age by 67% in food insecure populations [28].

However, the order of magnitude by which a specific intervention can make a difference depends on the local context and, therefore, needs to be assessed. Hence, the Government of Sindh, Pakistan in collaboration with WFP launched a stunting prevention programme, in two districts of Sindh, Pakistan, consisting of a preventative nutrition-based approach of WSBP using the primary healthcare system. A cluster randomized-controlled trial (RCT), was conducted to determine the impact of the WSBP on weight gain during pregnancy, birth outcomes (i.e., LBW), and nutritional status (i.e., stunting, wasting, underweight, and anemia) of their infants at the age of 6 months. The study also determined the impact of the nutrition-based interventions (lipid-based nutrient supplements medium quantity and multi-micronutrient powders) on nutritional status of children 6–23 months and 24–59 months of age. Findings from these cohorts are presented elsewhere [29, 30].

Purpose

We aimed to assess the effectiveness of provision of WSBP to women during pregnancy on weight gain, birth outcome (reduction of LBW), and improvement in nutritional status (i.e., stunting, wasting, underweight, and anemia) of their infants at 6 months of age.

Methods

Study design and setting

A cluster randomized-controlled trial was conducted in Thatta and Sujawal Districts, Sindh, Pakistan from August 2014 to December 2016. The study districts are located in the southern part of the Sindh province. They are administratively subdivided into nine sub-districts (Talukas) and 55 Union Councils (UCs) with a population of 1.5 million. Union Council is the smallest administrative unit in Pakistan. Agriculture, fishing, and livestock are the three major sources of earning for the people of study area. Wheat, rice, and sugarcane are major crops of this district. According to a study conducted by Asian Development Bank, 79% of the population of the area is poor [31, 32].

Intervention

A monthly ration of 5 kg of WSB+ (i.e., 165 g/day) was provided to women during pregnancy and for the first 6 months of lactation. The WSB+ was prepared from heat treated wheat and soya beans, vitamins, and minerals (Table 1). The intervention was delivered through lady health workers (LHWs) program, a vital program of the government's primary health care system. Health education messages were

Table 1 Nutritional values in wheat soya blend plus

Nutrients values	WSB +
Daily ration (g/person/day)	167
Energy (kcal)	633
Protein (g)	29.1
Fat (g)	10.2
Calcium (mg)	683
Iron (mg)	13.9
Iodine (μg)	67
Vitamin A ($\mu\text{g RE}$)	842
Thiamine B1 (mg)	0.66
Riboflavin vitamin B2(mg)	1.03
Niacin (mg NE)	15.3
Vitamin C (mg)	168.9
Pantothenic vitB5 (mg)	3.4
Vitamin B6 (mg)	1.8
Folic acid (μg)	100
Vitamin B12 (μg)	3
Vitamin D (μg)	10.0
Selenium (μg)	49.3
Vitamin E (mg)	15.8
Zinc (mg)	11.2
Copper (mg)	0.6
Folate (μg)	288

also provided on product use and benefits, infant, and young child feeding practices and maternal nutrition by LHWs using group sessions at the time of supplements' distribution and home visits on monthly basis. The control group received routine standard of care.

Sample size and randomization

To calculate the sample size, we aimed to be able to detect a 25% difference in the prevalence of LBW between intervention and control groups. With a power of 0.80 and a statistical significance of P value 0.05, we calculated that a sample size of 1000 per study group would be sufficient for assessing the reduction in LBW. The baseline prevalence of LBW (25%) in Sindh was assumed from the Pakistan Demographic Health Survey 2012-13.

The unit of randomization was a UC. Each UC has at least one public-sector healthcare facility and 15–20 LHWs affiliated with the facility. Of the 29 UCs, where the stunting prevention programme was implemented, 12 UCs were randomly allocated to intervention and control groups with a computer-generated randomization sequence that was generated by an independent expert at the Data Management Unit in AKU. Clusters were matched based on percentage of pregnant women and population size.

Study participants

All pregnant women who were participants in the stunting prevention programme were eligible to enrol in the study. The LHW family register and social mapping approach was used to identify pregnant women in their first trimester (< 12 weeks of gestation), second trimester (13–27 weeks of gestation), and third trimester (≥ 28 weeks of gestation) to recruit in the study. The enrolled pregnant women were followed during their pregnancy and for the first 6 months of lactation. Additionally, children (live born) of these women were also followed for the first 6 months of life.

Data collection

A household questionnaire was used to collect baseline information from PLW on socio-demographic characteristics, gestational age, reproductive history, antenatal care, morbidity, and care seeking practices, exposure to interventions, and anthropometry by data collection team. Baseline hemoglobin level of mothers was also assessed. A total of six data collection teams were hired locally from the study area. One data collection team was comprised of four female data collectors and one male team leader. The minimum qualification for data collectors was a 12th grade education and for the team leader was a 14th grade education.

The data collection teams received a 6-day hands-on training on data collection techniques, anthropometric measurements, hemoglobin testing, ethical issues, and data collection tools. A 1-day field testing was carried out before the actual field work. A study manual was provided to each team leader, which included instructions, methodology, and sampling strategy. All questionnaires were pre-tested in the field and changes were incorporated accordingly before actual data collection. Data were collected manually on hard copies of study questionnaires.

Monthly follow-ups were conducted to assess compliance to the intervention, pregnancy outcomes, and maternal and child morbidity, and mortality. Data on compliance were collected using participant recall and observation of used, and unused packets in targeted households during each visit. Anthropometric data of PLW and their infants were collected through Seca anthropometry kits on a quarterly basis. Hemoglobin levels in infants at 6 months of age were measured by a finger prick assay with HemoCue Hb 301 analyser.

For quality assurance, a monitoring team (separate from the data collectors) randomly visited 5% of households assessed by the data collection team to validate the collected data. The data collection process was supervised and monitored by team leaders, a field supervisor, and a study manager. ENA-SMART software was used to conduct plausibility checks for anthropometric measurements by the study supervisors on a weekly basis.

Data analysis

Analysis was performed using univariate and multivariate methods. The primary outcomes were weight gain during pregnancy, birth weight, child nutritional status (stunting, wasting, and underweight), and anemia at 6 months of age. Hemoglobin was measured in g/dL and Hb < 11 g/dL was used as a cut-off for classification of anemia among infants at 6 months of age. Descriptive statistics were obtained as mean, standard deviation, frequency, and proportions. The outcome analysis is adjusted for clustering effect using generalized linear model (GLM). Log (link) and Gaussian (link) functions were used for binary and linear outcomes, respectively. The analysis further adjusted for confounding factors including women age, education, baseline height, weight, BMI, gestational age, anemia status, early initiation of breastfeeding, and exclusive breastfeeding for 6 months. Significance has been defined as *P* value < 0.05 unless stated otherwise. Data were double entered by trained data input operators in Visual FoxPro database. All analysis was performed in STATA version 16.

Ethical considerations

The Ethics Review Committee of Aga Khan University granted approval for the study. Furthermore, the National Bioethics Committee of Pakistan approved the study for human subject research. Written informed consent was obtained from all participants at the time of enrolment in the study. The study was registered in ClinicalTrials.gov with registration number NCT02422953 on April 15, 2015.

Results

Baseline characteristics of study participants

A total of 2030 pregnant women (1017 in control group; 1013 in intervention group) were enrolled in the study and followed during pregnancy and the first 6 months of lactation. Overall, 93% of PLW completed the study. A total of 135 PLW (7%–70 in the control group; 65 in the intervention group) were lost to follow-up due to migration (3.6%), refusal (1%), and false pregnancy (1.8%) during the study period (Fig. 1).

The mean age of PLW was 29 years in both control and intervention groups. Approximately 19% of PLW, in both control and intervention groups, were enrolled before 12 weeks of gestation (first trimester), 55% were enrolled during 13–27 weeks of gestation (second trimester), and 25% of PLW were enrolled during the third trimester. At baseline, the mean gestational age was 21 weeks in both control and intervention groups. Additionally, there was no significant difference in the mean height between groups at baseline (154.4 ± 5.5 cm in controls versus 154.8 ± 5.4 cm in intervention) and mean weight (49.2 ± 7.9 kg in control versus 50.4 ± 8.4 kg in intervention). There was no difference in underweight among pregnant women ($\text{BMI} < 18.5 \text{ kg/m}^2$) (23.9% vs. 20.0%) and MUAC (24.1% vs. 24.4%) in the control as compared with intervention group. Similarly, household food consumption score and household hunger scale were not different in the control group compared with intervention group, respectively (Table 2).

Fig. 1 CONSORT flow diagram

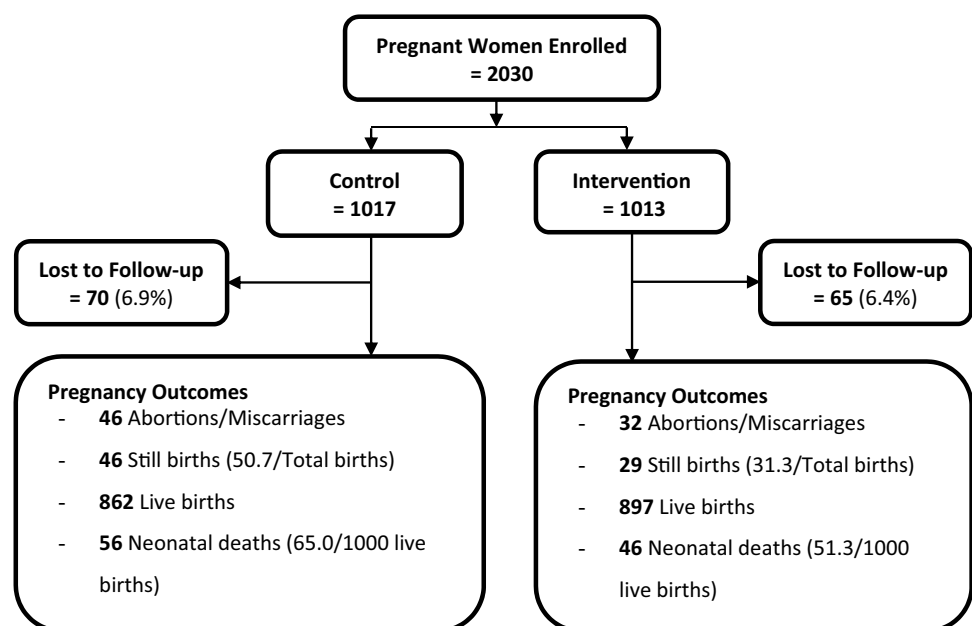


Table 2 Baseline characteristics of pregnant women at enrolment

Background characteristics	Control (N= 1017)	Intervention (N= 1013)
Age of pregnant women		
15–18 years	28 (2.8)	18 (1.8)
19–25 years	268 (26.4)	281 (27.7)
> 25 years	721 (70.9)	714 (70.5)
Mean age \pm SD	29.7 \pm 6.7	29.2 \pm 6.1
Gestational age in trimester		
First trimester (1–12 weeks)	200 (19.7)	192 (19.0)
Second trimester (13–27 weeks)	567 (55.8)	562 (55.5)
Third trimester (28 or more weeks)	250 (24.6)	259 (25.6)
Mean gestational age (weeks)	21.4 \pm 8.8	21.6 \pm 8.8
Body mass index (BMI) (kg/m ²)		
< 18.5	243 (23.9)	203 (20.0)
18.5–20.0	232 (22.8)	218 (21.5)
20.0–25.0	448 (44.1)	499 (49.3)
> 25.0	94 (9.2)	93 (9.2)
Women's educational status		
Illiterate	926 (91.1%)	811 (80.1%)
Literate	91 (8.9%)	202 (19.9%)
Parity		
0	160 (15.7%)	159 (15.7%)
1	156 (15.3%)	174 (17.2%)
2	167 (16.4%)	164 (16.2%)
3	120 (11.8%)	121 (11.9%)
> =4	414 (40.7%)	395 (39.0%)
Mean \pm SD no. of pregnancies	4.8 \pm 3.2	4.6 \pm 3.0
Anthropometry		
Height (cm) mean \pm SD	154.4 \pm 5.5	154.8 \pm 5.4
Weight (kg) mean \pm SD	49.2 \pm 7.9	50.4 \pm 8.4
MUAC (cm) mean \pm SD	24.1 \pm 2.6	24.4 \pm 2.7
Anemia status (Hb < 11 gm/dL)		
Hemoglobin < 11 gm/dl	852 (83.8)	794 (78.5)
Food consumption score		
Poor (1–28)	4 (0.4%)	2 (0.2%)
Borderline (28.1–42)	4 (0.4%)	9 (0.9%)
Acceptable (> 42)	1009 (99.2%)	1002 (98.9%)
Household hunger scale		
None or light hunger (0–1 score)	905 (89.0%)	921 (90.9%)
Moderate hunger (2–3 scores)	106 (10.4%)	90 (8.9%)
Severe hunger (4–6 scores)	6 (0.6%)	2 (0.2%)

Compliance of PLW to WSB + during pregnancy and lactation

Table 3 describes the compliance of PLW to WSB + reported in days during pregnancy and the first 6 months of lactation. The mean compliance of WSB + during pregnancy was 70.8 \pm 32.2 days and compliance during pregnancy and lactation period was 65.8 \pm 25.3 days. Approximately 91%

of PLW mentioned sharing their WSB + with other family members at least once during the study. Furthermore, 15% of women refused or stopped using WSB + due to undesirable taste (9.4%), or perceived side effects such as diarrhoea (1.8%), vomiting (1.6%), and abdominal pain (2.4%).

Pregnancy outcomes

There were three deaths (one in the intervention group and two in the control group) among pregnant women. In total, 1759 live births were reported during the study. Out of the live births, 17 women gave birth to twins. The still-birth rate was significantly higher ($P=0.045$) in the control group (50.7/1000 total births) than the intervention group (31.3/1000 total births). More newborns died during the first 28 days of life was higher in the control group (65.0/1000 live births) compared to the intervention group (51.3/1000 live births) (Fig. 1, Table 4).

Weight gain among pregnant women and low birthweight

Overall, maternal weight gain during pregnancy was no different among pregnant women receiving WSB + in control group (306.9 g/week, 95% CI 279.9–333.9) as compared to intervention group (326.7 g/week, 95% CI 315.2–338.1, $P=0.192$). No difference was observed in maternal BMI at end line (13.8%, 95% CI 12.4–15.1 vs. 14.6% 95% CI 13.8–15.5, $P=0.310$) in intervention and control group, respectively. Similarly, there was no differences revealed in the prevalence of LBW (34.0%, 95% CI 31.7–36.4 vs. 34.3% 95% CI 27.2–41.5, $P=0.932$) in intervention and control group, respectively. We enrolled 2030 pregnant women, but birthweight was only collected for 452 newborns. Due to the small-sample size, these results should be interpreted with caution as there was insufficient data collected on newborn birthweight by LHWs during the study (Table 5).

Nutritional status of infants at 6 months of age

There was a significant impact found on the prevalence of stunting ($n=1319$), wasting ($n=1330$), underweight ($n=1295$), and anemia ($n=1329$) in infants at 6 months of age whose mothers had received WSB throughout their pregnancy and the first 6 months of lactation. A significant reduction of 15% was observed in risk of stunting (RR 0.85, 95% CI 0.73–0.99; $P=0.041$) in infants in the intervention group as compared to control. There was also a significant reduction in risk of wasting (RR 0.77, 95% CI 0.65–0.91; $P=0.003$) and underweight (RR 0.77, 95% CI 0.69–0.87; $P<0.001$) among infants in intervention group. There is significant reduction in the risk of being anemic (RR 0.95, 95% CI 0.91–0.99; $P=0.02$) in the intervention

Table 3 Compliance of PLW to WSB+ during pregnancy and lactation

Indicators	Compliance during pregnancy (<i>n</i> = 1001)	Compliance during pregnancy and lactation (<i>n</i> = 849)
Mean compliance of WSB+ in days (days consumed/days participated in the study 100)	70.8 ± 32.2	65.8 ± 25.3
Sharing of WSB+ with family at least once	680 (67.9%)	772 (90.9%)
Reasons of refusal/stop or not using WSB+		
Taste is not good/bad taste	52 (5.2%)	80 (9.4%)
It causes diarrhoea	8 (0.8%)	15 (1.8%)
It causes vomiting	10 (1.0%)	14 (1.6%)
It causes abdominal pain	5 (0.5%)	20 (2.4%)

Table 4 Impact on pregnancy outcomes

Outcome	Control <i>N</i> = 947	Intervention <i>N</i> = 948	RR (95% CI) ^a	<i>P</i> value
Abortions/miscarriages	46	32	0.69 (0.45–1.08)	0.104
Still births	46	29	0.63 (0.4–0.99)	0.045
Neonatal deaths	56	46	0.82 (0.56–1.2)	0.306

^aThe analysis is adjusted for clustering using generalized linear model

group as compared to the control group (Table 6). After adjustment with different factors (cluster, maternal age, education, gestational age, baseline BMI, baseline anemia status of mother, early initiation of breastfeeding, and exclusive breastfeeding for 6 months), no evidence was noted on reduction in the risk of stunting among infants at 6 months of age in the intervention as compared to the control group (RR 0.91, 95% CI 0.78–1.07, *P* = 0.253) (Table 7).

Discussion

Our study demonstrates that the provision of WSB+ to PLW during pregnancy and the first 6 months of lactation had a significant impact on reductions in the risk of stunting (RR 0.85, 95% CI 0.73–0.99; *P* = 0.041), wasting (RR 0.77, 95% CI 0.65–0.91; *P* = 0.003), and underweight (RR 0.77, 95% CI 0.69–0.87; *P* < 0.001) in infants at 6 months of age. Similar results were also observed in Burundi, where a significant protective effect on stunting was seen in children born to mothers who received specialized nutritious foods [corn soy blend (CSB) and micronutrient fortified vegetable oil] [33]. Our results for reduction in anemia are comparable with Burundi study [33], where a significant protective effect on anemia among children (6.1 percentage points; 95% lower CI 0.3 percentage points) and mothers who gave birth in the previous 3 months (34.9% points; 95% lower CI 14.9% points). A food-based supplementation program for mothers during pregnancy and lactation and children 6–23 months in Guatemala significantly reduced the prevalence of stunting in children by 11.1% (*P* = 0.01) through family food rations

Table 5 Impact on weight gain during pregnancy and pregnancy outcomes

Indicators	Adjusted means ^b		<i>P</i> value
	Control	Intervention	
Weight gain during pregnancy (g/week) ^a	<i>N</i> = 507	<i>N</i> = 496	
Mean	306.9	326.7	0.192
95% CI	279.9–333.9	315.2–338.1	
Low birthweight (< 2.5 kg)	<i>N</i> = 127	<i>N</i> = 325	
Proportion	34.3	34.0	0.932
95% CI	27.2–41.5	31.7–36.4	
Body mass index < 18.5 (kg/m ²) end line	<i>N</i> = 993	<i>N</i> = 1001	
Proportion	14.6	13.8	0.310
95% CI	13.8–15.5	12.4–15.1	

^aWeight before delivery–first weight measurement of second trimester/duration of follow-up in week

^bThe analysis is adjusted for clustering and controlled for respective baseline measurements using generalized linear model

Table 6 Nutritional status of infants at 6 months of age (unadjusted)

Nutrition status	Unadjusted means ^a		RR (95% CI)	P value
	Control	Intervention		
Stunting	(N=617) 28.4	(N=702) 24.1	0.85 (0.73–0.99)	0.041
95% CI	(25.1–31.6)	(21.6–26.6)		
Wasting	(N=625) 29.3	(N=705) 22.6	0.77 (0.65–0.91)	0.003
95% CI	(27.0–31.6)	(19.2–26.0)		
Underweight	(N=601) 45.5	(N=694) 35.2	0.77 (0.69–0.87)	<0.001
95% CI	(43.3–47.6)	(31.4–39.0)		
Anemic (< 11 gm/dL)	(N=628) 86.0	(N=701) 81.7	0.95 (0.91–0.99)	0.024
95% CI	82.8–89.2	79.8–83.7		

^aThe analysis is adjusted for clustering using generalized linear model

Table 7 Nutritional status of infants at 6 months of age (adjusted)

Nutrition status	Adjusted means ^a		Adjusted RR (95% CI)	P value
	Control	Intervention		
Stunting	(N=617) 26.6	(N=701) 24.3	0.91 (0.78–1.07)	0.253
95% CI	(23.4–29.8)	(21.7–26.8)		
Wasting	(N=625) 28.5	(N=704) 23.4	0.82 (0.70–0.96)	0.013
95% CI	(26.3–30.8)	(20.2–26.6)		
Underweight	(N=601) 44.2	(N=693) 35.9	0.81(0.71–0.93)	0.002
95% CI	(41.3–47.0)	(32.0–39.8)		
Anemia (Hb < 11 gm/dL)	(N=628) 86.3	(N=700) 81.6	0.94 (0.91–0.98)	0.002
95% CI	83.7–89.0	79.8–83.3		

^aThe analysis is adjusted for clustering and controlled for several covariates (maternal age, education, gestational age, baseline BMI, baseline anemia status of mother, early initiation of breastfeeding, and exclusive breastfeeding for 6 months) using generalized linear model

(rice, beans, and oil) and CSB and 6.5% ($P < 0.05$) through family food rations and MNP [34].

Our results are similar to the studies conducted in Bangladesh and Ghana [35, 36]. In Bangladesh, children born to mothers receiving (lipid-based nutrient supplement) LNS had higher birth weights ($P = 0.007$), weight-for-age Z scores ($P = 0.006$), and length-for-age Z scores ($P = 0.035$) than children born to mothers receiving iron folic acid supplementation [35]. LNS provided to PLW also reduced the risk of stunting (RR 0.83; 95% CI 0.71, 0.97) among their children 14 days after delivery. However, when LNS was provided during pregnancy, lactation, and infancy in Ghana, children were found to have a significantly greater length-for-age Z score at 18 months of age (-0.69 ± 1.01) as compared to iron folic acid supplementation (-0.87 ± 0.99) and

multi-micronutrient supplements (-0.91 ± 1.01) ($P = 0.009$) [36]. Though our study was not designed to investigate the impact of WSB+ on reducing the risk of poor pregnancy and birth outcomes, but study was able to show a significant decrease in poor pregnancy outcomes (stillbirths and neonatal deaths) in the intervention group as compared to the control group. Multiple systematic reviews and meta-analyses have also confirmed the positive effect of nutritional supplementation (balanced energy-protein supplements) on pregnancy, birth, and neonatal outcomes [22, 23, 37, 17].

In Cambodia, nutritional supplementation (CSB Plus— a maize and soybean flour that is fortified with a vitamin and mineral premix) consumed by women during pregnancy resulted in a significant decrease in preterm birth (OR 0.33; 95% CI 0.12–0.89) and maternal anemia (OR

0.51; 95% CI 0.34–0.77) [24]. There was no difference in the rate of LBW between study groups (OR 0.65; 95% CI 0.33–1.26) in Cambodia. A similar lack of difference (RR 0.992; 95% CI 0.843–1.166; $P = 0.918$) was observed in LBW newborns in our study. Similarly, no difference was observed in weight gain among pregnant Cambodian women. In our study, birthweight was measured by LHWs within 72 h of birth. Although planned as part of the study protocol, this was found to be a limitation as LHWs were unable to weigh the newborns due to large distances and their involvement in polio campaigns. Unlike our study, no significant difference was observed in stillbirths in Cambodian study [24].

Our study has many strengths, such as the study was conducted in existing health system and the intervention was delivered through the existing government supported LHW programme. However, there are a few limitations. First, sharing of WSB + with other family members may have limited the impact on birth outcomes and nutritional status of infants at 6 months of age whose mothers received WSB +. Finally, the scarcity of birthweight may be a limitation of our study. Although we enrolled 2030 pregnant women, but only 452 newborns were weighted by the LHW. Considering the small-sample size, this study may have been unable to detect an effect of WSB + consumed by PLW on LBW in newborns.

The results of the study revealed that the provision of WSB + during pregnancy and the first 6 months of lactation is effective in lowering the risk of under nutrition and anaemia in infants at 6 months of age. Moreover, the provision of WSB + to PLW significantly reduced the risk of stillbirths. These results support the conclusion that nutritional supplements provided during pregnancy and lactation can be an effective strategy to reduce the risk of poor birth outcomes, and poor nutritional status of children, especially for undernourished pregnant mothers living in vulnerable settings. It is highly recommended to scale up this intervention package in Pakistan, especially for marginalized population.

Acknowledgements The authors would like to thank all the study participants for the participation. We also thank data collection teams, data management unit, grants, and administrative staff for their hard work. The authors' responsibilities were as follows: SS was PI of the study and designed the study design, and reviewed and interpreted the data; ZAB reviewed study design and final draft of the manuscript. GNK: supervised data collection activities and wrote the first draft of manuscript; MS and AR: contributed in data analysis; SA, SK, CG, SdeP, and MJ critically reviewed the manuscript. All authors reviewed and approved the final manuscript.

Funding World Food Programme, Islamabad, Pakistan.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

References

1. Abu-Saad K, Fraser D (2010) Maternal nutrition and birth outcomes. *Epidemiol Rev* 32:5–25
2. Couperus JW, Nelson CA (2006) Early brain development and plasticity. In: McCartney K, Phillips D (eds) *The Blackwell handbook of early childhood development*. Blackwell, MA, USA, pp 85–105
3. Khan Y, Bhutta ZA (2010) Nutritional deficiencies in the developing world: current status and opportunities for intervention. *Podiatry Clin N Am* 57:1409–1441
4. Black RE, Victora CG, Walker SP et al (2013) Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 382:427–451
5. Bhutta ZA, Ahmed T, Black RE et al (2008) What works? Interventions for maternal and child undernutrition and survival. *Lancet* 371:417–440
6. Devakumar D, Fall CH, Sachdev HS, Margetts BM, Osmond C, Wells JC, Costello A, Osrin D (2016) Maternal antenatal multiple micronutrient supplementation for long-term health benefits in children: a systematic review and meta-analysis. *BMC Med* 14:90
7. Dewey KG, Begum K (2011) Long-term consequences of stunting in early life. *Matern Child Nutr* 7:5–18
8. Victora CG, de Onis M, Hallal PC, Blossner M, Shrimpton R (2010) Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics* 125:e473–e480
9. Adair LS, Fall CH, Osmond C et al (2013) Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* 382:525–534
10. Olofin I, McDonald CM, Ezzati M, Flaxman S, Black RE, Fawzi W, Caulfield LE, Danaei G (2013) Nutrition impact model study associations of suboptimal growth with all-cause and cause-specific mortality in children under 5 years: a pooled analysis of ten prospective studies. *PLoS ONE* 8:e646–e636
11. Prentice AM, Ward KA, Goldberg GR, Jarjou LM, Moore SE, Fulford AJ, Prentice A (2013) Critical windows for nutritional interventions against stunting. *Am J Clin Nutr* 97:911–918
12. Leroy JL, Ruel M, Habicht JP, Frongillo EA (2014) Linear growth deficit continues to accumulate beyond the first 1000 days in low- and middle-income countries: global evidence from 51 national surveys. *J Nutr* 144:1460–1466
13. Lundeen EA, Stein AD, Adair LS et al (2014) Height-for-age Z scores increase despite increasing height deficits among children in five developing countries. *Am J Clin Nutr* 100:821–825
14. The International Bank For Reconstruction and Development (2006) repositioning nutrition as central to development a strategy for large-scale action. <https://siteresources.worldbank.org/NUTRITION/Resources/281846-1131636806329/NutritionStrategy.pdf>. Accessed 26 March 2019.
15. Kramer MS, Kakuma R (2003) Energy and protein intake in pregnancy. *Cochrane Database Syst Rev* 4:32
16. Ceesay SM, Prentice AM, Cole TJ, Foord F, Poskitt EME, Weaver LT, Whitehead RG (1997) Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomized controlled trial. *BMJ* 315:786–790
17. Imdad A, Bhutta ZA (2011) Effect of balanced protein energy supplementation during pregnancy on birth outcomes. *BMC Public Health* 11:17
18. World Health Organization (2012) WHO Guideline: daily iron and folic acid supplementation in pregnant women geneva. World Health Organization, Geneva, p 27
19. Fall CHD, Fisher DJ, Osmond C, Margetts BM (2009) Multiple micronutrient supplementation during pregnancy in low-income

- countries: a meta-analysis of effects on birth size and length of gestation. *Food Nutr Bull* 30:S533–S546
20. Margetts BM, Fall CHD, Ronsmans C, Allen LH, Fisher DJ (2009) Maternal micronutrient supplementation study group multiple micronutrient supplementation during pregnancy in low-income countries: review of methods and characteristics of studies included in the meta-analyses. *Food Nutr Bull* 30(7):S526
 21. Haider BA, Yakoob MY, Bhutta ZA (2011) Effect of multiple micronutrient supplementation during pregnancy on maternal and birth outcomes. *BMC Public Health* 11:S19
 22. Stevens B, Buettner P, Watt K, Clough A, Brimblecombe J, Judd J (2015) The effect of balanced protein energy supplementation in undernourished pregnant women and child physical growth in low- and middle-income countries: a systematic review and meta-analysis. *Matern Child Nutr* 11:415–432
 23. Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D (2015) Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database Syst Rev* 6:32
 24. Janmohamed A, Karakochuk CD, Boungnasiri S, Chapman GE, Janssen PA, Brant R, Green TJ, McLean J (2016) Prenatal supplementation with corn soya blend plus reduces the risk of maternal anemia in late gestation and lowers the rate of preterm birth but does not significantly improve maternal weight gain and birth anthropometric measurements in rural cambodian women: a randomized trial. *Am J Clin Nutr* 103:559–566
 25. World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. <https://apps.who.int/iris/bitstream/handle/10665/250796/9789241549912-eng.pdf;jsessionid=C01C1A267A8455401C2BFA47E548FF5B?sequence=1>. Accessed 26 Mar 2019
 26. Bhutta ZA, Das JK, Rizvi A et al (2013) Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* 382:9890
 27. Imdad A, Yakoob MY, Bhutta ZA (2011) Impact of maternal education about complementary feeding and provision of complementary foods on child growth in developing countries. *BMC Public Health* 11(3):S25
 28. Lassi ZS, Das JK, Zahid G, Imdad A, Bhutta ZA (2013) Impact of education and provision of complementary feeding on growth and morbidity in children less than 2 years of age in developing countries: a systematic review. *BMC Public Health* 13(3):S13
 29. Soofi S, Nawaz G, Garzon C (2019) Effect of lipid-based nutrient supplement-medium quantity on reduction of stunting in children 6–23 months of age in Sindh, Pakistan: a cluster randomized controlled trial current developments in nutrition. *Nutrition* 3:5–25
 30. Impact of nutrition supplementation programme within the primary healthcare system to prevent stunting among children under 5 years in Thatta and Sujawal districts, Sindh, Pakistan: cross-sectional surveys. Unpublished manuscript, Aga Khan University, Karachi, Pakistan.
 31. Sindh Coastal and inland community development project (2005) Asian Development Bank, Project No. 37188, Tech Ass Consultant Rep Vol-II. <https://www.adb.org/projects/37188-013/main>
 32. Khan SB, Ahmad M, Sadaf M, Kashif M, Hamid R (2009) Crops Area And Production (By Districts) (1981-82 TO 2008-09)
 33. Leroy JL, Olney D, Ruel M (2018) Tubaramure, a food-assisted integrated health and nutrition program, reduces child stunting in Burundi: a cluster-randomized controlled intervention trial. *J Nutr* 148:445–452
 34. Olney D, Leroy JL, Bliznashka L, Ruel M (2018) PROCOMIDA, a food-assisted maternal and child health and nutrition program, reduces child stunting in Guatemala: a cluster-randomized controlled intervention trial. *J Nutr* 148:1493–1505
 35. Mridha MK, Matias SL, Chaparro CM et al (2016) Lipid-based nutrient supplements for pregnant women reduce newborn stunting in a cluster-randomized controlled effectiveness trial in Bangladesh. *Am J Clin Nutr* 103:236–249
 36. Adu-Afarwuah S, Lartey A, Okronipa H, Ashorn P, Peerson JM, Arimond M, Ashorn U, Zeilani M, Vosti S, Dewey KG (2016) Small-quantity, lipid-based nutrient supplements provided to women during pregnancy and 6 month postpartum and to their infants from 6 month of age increase the mean attained length of 18-month-old children in semi-urban Ghana: a randomized controlled trial. *Am J Clin Nutr* 104:797–808
 37. Gresham E, Byles JE, Bisquera A, Hure AJ (2014) Effects of dietary interventions on neonatal and infant outcomes: a systematic review and meta-analysis. *Am J Clin Nutr* 100:1298–1321