Original Article

Antenatal iron–folic acid supplementation reduces risk of low birthweight in Pakistan: secondary analysis of Demographic and Health Survey 2006–2007

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Abstract

The aim of the current study was to examine the impact of antenatal iron–folic acid (IFA) supplementation on perceived birth size and birthweight in Pakistan over a 5-year period from 2002 to 2006. The data source was the Pakistan Demographic and Health Survey (PDHS) 2006–2007. Information from 5692 most recent live-born infants within 5 years prior to the survey was examined. The primary outcomes were maternal perception of birth size and birthweight, and the main exposure was any use of antenatal IFA supplements. Birthweight was reported for only 10% of the live births in the PDHS 2006–2007. Multivariate logistic regression analysis was adjusted for the cluster sampling design and for 13 potential confounders. The risk of having smaller than average birth size newborn was significantly reduced by 18% (adjusted odds ratio 0.82, 95% confidence interval 0.71, 0.96) for mothers who used any IFA supplements compared with those who did not. A similar (18%), but non-significant reduction in the risk of low birthweight, was found with the maternal use of IFA supplements. The risk of having smaller than average birth size babies was significantly reduced by 19% in those women who started IFA in the first trimester of pregnancy. About 11% of babies with smaller than average birth size were attributed to non-use of antenatal IFA supplements. Antenatal IFA supplementation significantly reduces the risk of a newborn of smaller than average birth size in Pakistan. Universal coverage of supplementation would improve birth size.

Keywords: birth size, birthweight, antenatal iron–folic acid supplements, Pakistan, Demographic and Health Survey.

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Introduction

Every year 20 million infants are born with low birthweight (LBW; birthweight <2500 g) globally. The majority of the LBW infants are in two regions of the world: Asia and Africa. The situation in the South Central Asia is even worse where about 11 million infants are born with LBW each year (UNICEF & WHO 2004). The primary causes of LBW are preterm

birth, intrauterine growth restriction or a combination of both (Kramer 1987). LBW affects the immediate and long-term health and survival of newborns (Christian 2010). Despite having made significant progress in incorporating maternal and newborn care into the national policies and programmes during the last decade in Pakistan (Khan *et al.* 2012), the prevalence of LBW infants has remained high (UNICEF & WHO 2004; UNICEF *et al.* 2011).

Anaemia during pregnancy is a major global public health problem as 42% of the pregnant women are anaemic (World Health Organization & Centers for Disease Control and Prevention 2008), while the situation in Pakistan is even worse where 51% of the pregnant women have anaemia at any stage during their pregnancy (UNICEF *et al.* 2011). Iron deficiency is the most common cause of the anaemia during pregnancy and it is the most widespread nutritional deficiency in the world (Stoltzfus & Dreyfuss 1998). The World Health Organization (2012) recommends a standard daily oral prophylactic dose of 30–60 mg of iron and 400 µg of folic acid supplements throughout pregnancy. In Pakistan, like other low- and middle-income countries, iron–folic acid (IFA) supplements (elemental iron 60 mg and folic acid 0.5 mg) are distributed by the maternal and child health services through the existing primary health care system including community health workers and health facilities. However, the findings of the latest Pakistan Demographic and Health Survey (PDHS) 2006–2007 revealed that only 43% of pregnant women consumed any IFA supplements in their most recent pregnancy [National Institute of Population Studies (NIPS) [Pakistan] & Macro International Inc 2008].

Anaemia during pregnancy increases the risk of LBW babies (Sekhavat *et al.* 2011; Zanini *et al.* 2011), and LBW has been recognized as one of the major risk factors for neonatal mortality (Yasmin *et al.* 2001; Lawn *et al.* 2005; Titaley *et al.* 2008; Zanini *et al.* 2011). The fourth Millennium Development Goal (MDG4) aims to reduce under five deaths by two-thirds by 2015 (UNICEF *et al.* 2013). To achieve MDG4 targets,

it is important to improve neonatal survival, which accounts for 40% of under five deaths worldwide (Oestergaard *et al.* 2011). Pakistan has the world third highest number of neonatal deaths (Khan *et al.* 2012). Our previous secondary analyses of PDHS 2006–2007 showed an association between smaller than average birth size (a surrogate for LBW) and neonatal mortality in Pakistan (Nisar & Dibley 2014). The aim of the current study was to examine the impact of antenatal IFA supplementation on perceived birth size and birthweight in Pakistan over a 5-year period from 2002 to 2006.

Materials and methods

Data source

Data for the current study were derived from the PDHS 2006–2007, which is a nationally representative sample of Pakistan. The details of the sampling technique have been described elsewhere (Macro International 1996). Briefly, a stratified, multistage cluster sampling method was used in the PDHS 2006–2007. Urban and rural samples were drawn separately and in proportion to the population of each province. At the first stage, clusters with a probability proportional to size were selected. In urban areas, clusters were selected from the enumeration blocks, each including 200–250 households. Lists of villages enumerated in the 1998 population census were used to select clusters in the rural areas. In the second stage, 105 households were selected using a systematic random sampling technique to conduct interviews for Women's Questionnaire [National Institute of

Key messages

- Despite a significant progress in incorporating maternal and newborn care into the national policies and programs, the prevalence of low birth weight (LBW) infants has remained high in Pakistan.
- Use of antenatal iron-folic acid (IFA) reduced the risk of smaller than average birth size/LBW infants in Pakistan. The greatest protective effect of IFA was seen when initiated IFA in the first trimester of pregnancy.
- Non-use of antenatal IFA attributed 11% of smaller than average birth size. With universal coverage of antenatal IFA, 112000 Pakistani newborns could be prevented from having smaller than average birth size annually.

Population Studies (NIPS) [Pakistan] & Macro International Inc 2008].

PDHS 2006–2007 used six types of questionnaires: the Community, the Short Household, the Long Household, the Women's, the Maternal Verbal Autopsy and the Child Verbal Autopsy Questionnaires. The contents of the Household and Women's Questionnaires were based on the model questionnaires developed by the Measure DHS programme. The Women's Questionnaire collected information from ever-married women 15–49 years of age on background characteristics including education, literacy, native language and marriage characteristics; full birth history; history of antenatal care for the most recent birth within 5 years preceding the survey; delivery and post-natal care for all births as well as the survival of live-birth infants.

In the PDHS 2006–2007, the response rate of eligible women was high (95%). We selected only the last live births in the 5 years (2002–2006) immediately preceding the survey for the current study to avoid the violation of the independence assumption and reduce potential recall bias. In the survey, a verbal informed consent was taken from each respondent before the interview. The protocol of secondary analysis of PDHS was approved by the Human Ethics Committee of the University of Sydney, Australia.

Description of variables

Study outcomes

The main study outcome was the maternal perception of birth size of their last live births in the last 5 years prior to survey. The question asked in the PDHS for the perception of birth size was as follows: 'What was the size of the baby at birth?' It was recorded as the 'smallest', 'smaller than average', 'average', 'larger than average' and the 'largest'. We pooled these categories to form a binary variable as the 'larger than or equal to the average birth size' (including the largest, larger than average and average categories) and the 'smaller than average birth size' (including the smallest and smaller than average categories) to explore the association

between maternal use of antenatal IFA supplements and maternal perception of smaller than average birth size. As recommended by others (Channon 2011), we considered the perceived birth size as a proxy for the birthweight in our study.

As a secondary outcome, we also analysed a subsample of live births in the last 5 years prior to the survey, which recorded the birthweight (11%) in the PDHS 2006–2007. The question asked in the PDHS for birthweight was as follows: 'What was the weight of the baby at birth?' The reported birthweight was either based on a written record or the mother's recall. To investigate the effect of the exposure variable, we constructed three separate binary variables for the birthweight that were based on cut-off points of LBW as either <1500, <2000 or <2500 g, respectively, as the number of reported cases of birthweight was low. Further, three binary variables with three different cut-off points of birthweight help policy makers and programme managers to understand the effect of antenatal IFA on birthweight clearly.

Study exposure variable

The main study exposure variable was mother's reported use of any IFA supplements during the last pregnancy in the 5 years prior to survey. The questions asked in the PDHS related to the IFA supplements were standard DHS questions used in many other countries, and included 'During this pregnancy, were you given or did you buy any iron tablets or iron syrup?' and 'During the whole pregnancy, for how many days did you take the tablets or syrup?' A respondent was classified as using antenatal IFA supplements if she reported taking IFA tablets for at least a day during pregnancy (any IFA supplementation), although our analysis did not specifically analyse the number of days mothers took IFA supplements. The effect of starting supplements progressively later in pregnancy (first, second and third trimester) was also investigated using the date of the first antenatal health care examination as a surrogate for the start of IFA supplementation. Further, the isolated effect of IFA supplementation independent of any other antenatal care services was

Table 1. Description of variables used in the study

Variables	Description and categorization
Community level	
Place of residence	Place of residence (1 = urban; 2 = rural)
Region	Region (1 = Baluchistan; 2 = Khyber Pakhtunkhwa; 3 = Sindh; 4 = Punjab)
Socio-economic status	
Maternal education	Maternal education status (1 = secondary and above education; 2 = primary; 3 = no education)
Paternal education	Paternal education status (1 = secondary and above education; 2 = primary; 3 = no education)
Parental occupation	Maternal and paternal employment status (1 = mother without a job outside the home and father employed; 2 = mother and father both employed; 3 = father unemployed)
Household wealth index	Composite index of household amenities (1 = richest; 2 = richer; 3 = middle; 4 = poorer; 5 = poorest)
Fuel used for cooking	Fuel used for cooking at home (1 = natural gas/electricity; 2 = biomass)
Maternal and newborn characteristics	
Maternal age at childbirth	Maternal age at childbirth (1 = 20–29 years; 2 = less than 20 years; 3 = 30 years and more)
Baby's gender	Gender of neonate (1 = female; 2 = male)
Outcome of last pregnancy	Outcome of last pregnancy (1 = singleton birth; 2 = multiple births)
Status of recorded birthweight	Status of recorded birthweight (1 = based on maternal recall; 2 = based on written record)
Birth rank	Birth rank of neonate (1 = 2nd or 3rd birth rank; 2 = 1st birth rank; 3 = ≥4th birth rank)
Desire for pregnancy	Intention to become pregnant (1 = wanted then; 2 = wanted later; 3 = wanted no more). In PDHS 2006–2007, the following question was asked to all women who had live births 5 years prior to the survey about the desire for pregnancy: 'At the time you became pregnant with (NAME), did you want to become pregnant then, did you want to wait until later or did you not want to have any (more) children at all?'
Any antenatal services	Any antenatal services used (1 = no; 2 = yes)
Any IFA supplementation	Any use of IFA supplementation (1 = no; 2 = yes)
Maternal-perceived birth size	Subjective assessment of the respondent on the birth size (0 = larger than or equal to average birth size; 1 = smaller than average birth size)
Birthweight	Three variables were constructed as: (1) birthweight (0 = ≥2500 g; 1 = <2500 g); (2) birthweight (0 = ≥2000 g; 1 = <2000 g); (3) birthweight (0 = ≥1500 g; 1 = <1500 g)

IFA, iron–folic acid; PDHS, Pakistan Demographic and Health Survey.

examined by constructing a combined variable as any IFA supplementation with other antenatal services.

Confounding factors

Other explanatory variables considered in the analyses are given in Table 1. We considered two community level, five socio-economic status, and five maternal and newborn characteristic variables in our analyses. Maternal-reported use of any antenatal care services during the last pregnancy within 5 years prior to survey was also included in the analyses.

The household wealth index was constructed from an inventory of household assets and facilities. The weighting values for the indicator variables were assigned using principal component analysis.

This index gives each household a score on each of the following variables: source of drinking water, toilet facilities, material of floor, availability of electricity, ownership of a radio, ownership of a TV, ownership of a refrigerator and means of transportation. The household wealth index was the sum of the weighted scores for each item (Filmer & Pritchett 2001). For analysis the household wealth index scores were ranked and divided into quintiles.

Statistical analysis

Data analysis was conducted using STATA 13.1 (StataCorp, College Station, TX, USA) with 'Svy' commands to allow for adjustments for the cluster sampling design used in the survey. The frequencies along with weighted percentage were calculated for

the study variables. Unadjusted analyses were carried out using logistic regression to identify the potential risk factors for having a newborn of smaller than average birth size. Afterwards, we constructed multivariate logistic regression models with a multistage technique to identify the independent risk factors for having a newborn of smaller than average birth size using step-wise backward elimination procedures. All variables with a $P \leq 0.2$ at univariate analyses were included in the multivariate models. First, we entered the community level and socio-economic variables into the baseline model, and only those that were significantly associated with having a newborn of smaller than average birth size ($P < 0.05$) were retained for the subsequent model. In the second stage, we added the maternal and newborn characteristic factors into the baseline model and only those that were significantly associated with having a newborn of smaller than average birth size ($P < 0.05$) were retained along with the significant community level and socio-economic status factors for the subsequent model. Afterward, use of antenatal health care services variable was included in the model with the significant community level, socio-economic, and maternal and newborn characteristic factors. Finally, variables related to the IFA supplementation – any IFA supplementation and timing of start of IFA supplements – were examined separately in the model with the significant community, socio-economic, maternal and newborn characteristics factors. Similar modelling techniques were employed on a subsample analysis to investigate the effect of IFA supplementation on birthweight. In addition, the birthweight models were also adjusted for the status of reported birthweight based on either maternal recall or written record. This variable was retained in all birthweight models. Adjusted odds ratios (aORs) and their 95% confidence intervals (CIs) derived from the adjusted multivariate logistic regression models were considered to examine the effect of the study factors on the perceived birth size and birthweight.

Population attributable risk (PAR) was calculated to assess the total risk of having a newborn of smaller than average birth size in the general population that was attributable to women who did not use IFA supplements during their pregnancy. We assumed that the

association between IFA supplementation and having a newborn of smaller than average birth size was causal and that removal of IFA supplementation had no effect on the distribution of other risk factors for having a newborn of smaller than average birth size. The following formula was used to calculate PAR (Rockhill *et al.* 1998; Natarajan *et al.* 2007; Rothman *et al.* 2012):

$$PAR = Pe \times [(aOR - 1)/aOR]$$

where Pe is the proportion of infants of smaller than average birth size associated with having a mother who did not use any IFA supplements. aOR is the adjusted odds ratio for having a newborn of smaller than average birth size who were born to women who did not use IFA supplements during their pregnancy (this aOR is the inverse of the value reported for women who did take IFA supplements). Based on our PAR estimates, the annual number of live births (Khan *et al.* 2012) and the incidence of LBW in Pakistan (UNICEF *et al.* 2011), we estimated the annual number of babies having smaller than average birth size that could be prevented with the universal use of antenatal IFA supplementation. However, PAR estimates depend on the prevalence of exposure that might vary across population.

Results

A total of 5692 (5639 weighted) live births in the last 5 years preceding the survey were selected. For babies who were weighed at birth, the number and mean birthweight of babies by maternal-perceived birth size, according to the PDHS 2006–2007 categories and according to the current study categories, are given in Table 2. The perceived birth size showed a close correspondence to the birthweight of babies in Pakistan. The mean birthweight was <2500 g in infants who were categorized as having smaller than average birth size.

The basic characteristics of the respondents are shown in Table 3. Nearly 70% of mothers were living in the rural areas at the time of the survey. About two-thirds of the sampled mothers had no education. Biomass energy was used by 70% of mothers as fuel

Table 2. For babies who were weighed at birth, number and mean ($\pm$ SE) birthweight by perceived birth size according to the PDHS 2006–2007 categories and according to the current study categories

Perceived birth size categories	<i>n</i> *	<i>n</i> †	Mean (g)	$\pm$ SE
According to PDHS 2006–2007				
Smallest	48	50	1771.8	$\pm$ 161.8
Smaller than average	115	113	2424.8	$\pm$ 76.7
Average	277	284	3065.4	$\pm$ 52.2
Larger than average	129	136	3332.9	$\pm$ 85.1
Largest	33	40	3969.3	$\pm$ 196.7
According to study variable				
Smaller than average birth size	163	163	2223.7	$\pm$ 83.7
Larger than or equal to average birth size	439	460	3222.6	$\pm$ 51.6

PDHS, Pakistan Demographic and Health Survey; SE, standard error. *Unweighted. †Weighting was applied to compensate for the multistage cluster sampling design.

for cooking at home. Almost all (99%) births were singleton in our sample. One in six live births was first-ranked infants. Nearly two-thirds of the mothers reported to use any antenatal care services during their last pregnancy. Any use of antenatal IFA supplementation was reported by 44% of mothers. Two-thirds of mothers (67%) reported that their babies had greater than or equal to average birth size. Birthweight was reported in 11% of live births and out of them, 0.6% had <1500 g birthweight, 1.3% had <2000 g and 2.7% had <2500 g birthweight.

The basic characteristics of respondents who reported birthweight, presented in Table 4, showed that 65% of them were living in urban communities and 52% were belonging to province Punjab. Nearly 29% of respondents were teenagers (<20 years) at the time of childbirth and slightly less than three-fifths of respondents (58%) had secondary or above education. Similarly, slightly less than three-quarters of fathers (72%) had secondary and above education. Fifty-five per cent of mothers were belonging to the richest household wealth index quintile, whereas only 6% were belonging to the poorest household wealth index quintile. About 63% of mothers reported to use natural gas/electricity as a fuel for cooking at home. Fifty-six per cent of babies were males. One out of five (21%) live births was first-ranked babies. A substantial majority (92%) of the respondents used any antenatal care services and three-quarters of respondents reported to use any IFA supplements during their pregnancy. Majority of women (81.6%) reported birthweight based on their recall.

The unadjusted and adjusted analyses for factors associated with risk of having smaller than average birth size in Pakistan are presented in Table 5. Multivariate logistic regression analyses showed that infants whose mothers were living in province Sindh or Baluchistan, had no education or primary level education, male infants, first-ranked infants, multiple births and whose mother did not want 'any more babies' had significantly higher odds of having a newborn of smaller than average birth size in Pakistan.

Mothers who used natural gas/electricity as fuel for cooking at home had significantly lower odds of having a newborn of smaller than average birth size compared with those who used biomass energy for cooking at home after adjustment for other confounding factors. The variable 'fuel use for cooking' was highly correlated with the variable 'household wealth index' and when we replaced it with the household wealth index variable in the final model, the household wealth index became significant without disturbing in the estimated effects of other variables (poorest quintile aOR: 1.42, 95% CI: 1.08, 1.88, $P = 0.011$).

The effect of IFA supplementation on the perceived birth size is presented in Table 6. Mothers who used any IFA supplements during their pregnancy had significantly lower adjusted odds of having a newborn of smaller than average birth size (aOR: 0.82, 95% CI: 0.71, 0.96, $P = 0.013$) than mothers who never used any IFA supplements. Mothers who started their IFA supplements in the first trimester of their pregnancy had significantly lower adjusted odds of having a newborn of smaller than average birth size

Table 3. Prevalence of community level, socio-economic status, and maternal and neonatal characteristics of the most recent live birth 5 years prior to the PDHS 2006–2007 ($n = 5692$)

Variables	n^*	$n^\dagger$	$\%^\dagger$	Variables	n^*	$n^\dagger$	$\%^\dagger$
Community level				Baby's gender			
Cluster type				Male	3062	3050	54.1
Urban	1986	1701	30.2	Female	2630	2589	45.9
Rural	3706	3938	69.8	Outcome of pregnancy			
Region/province				Singleton birth	5628	5580	99.0
Punjab	2290	3157	56.0	Multiple births	64	59	1.1
Sindh	1622	1399	24.8	Birth rank			
Khyber Pakhtunkhwa	1109	823	14.6	2nd or 3rd birth rank	1898	1912	33.9
Baluchistan	671	260	4.6	1st birth rank	983	961	17.1
Socio-economic status				≥ 4 th birth rank	2811	2766	49.1
Maternal education				Desire for pregnancy			
Secondary and above	1117	1149	20.4	Wanted then	4176	4107	72.8
Primary	781	845	15.0	Wanted later	754	742	13.2
No education	3794	3646	64.7	Wanted no more	752	779	13.8
Paternal education				Missing	10	11	0.2
Secondary and above	2680	2698	47.9	Any antenatal services used			
Primary	914	927	16.4	No	2002	1969	34.9
No education	2088	2006	35.6	Yes	3683	3665	65.0
Missing	10	8	0.1	Missing	7	5	0.1
Parental occupation				Any IFA supplementation			
Mother without a job outside the home and father employed	4166	4096	72.6	No	3119	3180	56.4
Mother and father both employed	963	982	17.4	Yes	2567	2455	43.5
Father unemployed	191	174	3.1	Missing	6	5	0.1
Missing	372	387	6.9	Perceived birth size			
Household wealth index				Smaller than average birth size	1957	1842	32.7
Richest	1013	1025	18.2	Larger than or equal to average birth size	3735	3798	67.3
Richer	1054	1052	18.7	Birthweight			
Middle	1109	1089	19.3	Low birthweight (<1500 g)	42	36	0.6
Poorer	1232	1191	21.1	Normal (≥ 1500 g)	560	587	10.4
Poorest	1284	1281	22.7	Missing	5090	5017	89.0
Fuel used for cooking				Birthweight			
Natural gas/electricity	1606	1445	25.6	Low birthweight (<2000 g)	79	73	1.3
Biomass energy	3858	3928	69.7	Normal (≥ 2000 g)	523	550	9.7
Missing	228	267	4.7	Missing	5090	5017	89.0
Maternal and newborn characteristics				Birthweight			
Maternal age at childbirth				Low birthweight (<2500 g)	163	152	2.7
20–29 years	2968	2976	52.8	Normal (≥ 2500 g)	439	471	8.3
Less than 20 years	2534	2482	44.0	Missing	5090	5017	89.0
30 and more	190	182	3.2				

IFA, iron–folic acid; PDHS, Pakistan Demographic and Health Survey. *Unweighted. $\dagger$ Weighting was applied to compensate for the multistage cluster sampling design.

(aOR: 0.81, 95% CI: 0.66, 0.99, $P = 0.044$) compared with those mothers who never used any IFA supplements. In contrast women starting IFA supplements later in the second or third trimester of pregnancy did not have a significant reduction in the adjusted odds of delivering a baby of smaller than average birth size (aOR: 0.88, 95% CI: 0.72, 1.07, $P = 0.188$). Further,

mothers who used any IFA supplements with or without any other antenatal care services had significantly lower adjusted odds of having a newborn of smaller than average birth size (aOR: 0.83, 95% CI: 0.69, 0.99, $P = 0.044$) than those who never used any other antenatal services and never used any IFA supplements during their pregnancy.

Table 4. Prevalence of community level, socio-economic status, and maternal and neonatal characteristics of the most recent live birth 5 years prior to the PDHS 2006–2007 with reported birth weight ($n=602$)

Variables	n^*	$n^\dagger$	$\%^\dagger$	Variables	n^*	$n^\dagger$	$\%^\dagger$
Community level				Baby's gender			
Cluster type				Male	325	350	56.3
Urban	415	408	65.4	Female	277	272	43.7
Rural	187	215	34.6	Outcome of pregnancy			
Region/province				Singleton birth	586	606	97.4
Punjab	271	325	52.1	Multiple births	16	16	2.6
Sindh	264	259	41.6	Status of reported birthweight			
Khyber Pakhtunkhwa	61	37	6.0	Based on maternal recall	485	509	81.7
Baluchistan	6	2	0.3	Based on written record	117	114	18.3
Socio-economic status				Birth rank			
Maternal education				2nd or 3rd birth rank	272	284	45.6
Secondary and above	345	360	57.8	1st birth rank	123	129	20.8
Primary	80	80	12.9	≥ 4 th birth rank	207	209	33.6
No education	177	183	29.3	Desire for pregnancy			
Paternal education				Wanted then	449	464	74.5
Secondary and above	433	449	72.1	Wanted later	92	92	14.8
Primary	74	69	11.1	Wanted no more	60	66	10.6
No education	94	104	16.7	Missing	1	1	0.2
Missing	1	1	0.2	Any antenatal services used			
Parental occupation				No	43	50	8.0
Mother without a job outside the home and father employed	474	502	80.7	Yes	558	572	91.9
Mother and father both employed	95	86	13.8	Missing	1	1	0.1
Father unemployed	10	11	1.7	Any IFA supplementation			
Missing	23	24	3.9	No	135	156	25.0
Household wealth index				Yes	467	467	75.0
Richest	334	343	55.0	Missing	6	5	0.1
Richer	108	103	16.6	Perceived birth size			
Middle	79	94	15.1	Smaller than average birth size	163	163	26.2
Poorer	52	49	7.9	Larger than or equal to average birth size	439	460	73.8
Poorest	29	34	5.5	Birthweight			
Fuel used for cooking				Low birthweight (<1500 g)	42	36	5.7
Natural gas/electricity	388	390	62.7	Normal (≥ 1500 g)	560	587	94.3
Biomass energy	182	199	32.0	Birthweight			
Missing	32	33	5.3	Low birthweight (<2000 g)	79	73	11.8
Maternal and newborn characteristics				Normal (≥ 2000 g)	523	550	88.2
Maternal age at childbirth				Birthweight			
20–29 years	391	420	67.5	Low birthweight (<2500 g)	163	152	24.3
Less than 20 years	187	179	28.7	Normal (≥ 2500 g)	439	471	75.7
30 and more	24	24	3.8				

IFA, iron–folic acid; PDHS, Pakistan Demographic and Health Survey. *Unweighted. † Weighting was applied to compensate for the multistage cluster sampling design.

Both fuel used for cooking at home and the antenatal IFA supplementation showed associations with the maternal perception of birth size in our sample. We constructed a combined variable of fuel used for cooking with the IFA supplementation to investigate the extent of protective effect of the combined variable. Our results showed that the magnitude of the

protective effect on the risk of having a newborn of smaller than average birth size was the highest (33%) among mothers who used natural gas/electricity as fuel for cooking at home and used any IFA supplements (aOR: 0.67, 95% CI: 0.53, 0.85, $P = 0.001$) compared with those who used biomass energy for cooking and never used any IFA supplements.

Table 5. Factors associated with smaller than average birth size in Pakistan: unadjusted and adjusted odds ratio using multivariate logistic regression models

Variables	Smaller than average birth size		Unadjusted			Adjusted*		
	<i>n</i> [†]	% [†]	OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>
Community level								
Cluster type								
Urban	531	31.2	1.00					
Rural	1311	33.3	1.10	(0.92, 1.31)	0.287			
Region/province								
Punjab	919	29.1	1.00			1.00		
Sindh	538	38.4	1.52	(1.27, 1.83)	0.000	1.52	(1.25, 1.85)	0.000
Khyber Pakhtunkhwa	277	33.6	1.24	(1.00, 1.53)	0.052	1.16	(0.93, 1.46)	0.180
Baluchistan	109	41.9	1.76	(1.33, 2.33)	0.000	1.66	(1.23, 2.24)	0.001
Socio-economic status								
Maternal education								
Secondary and above	303	26.4	1.00			1.00		
Primary	268	31.7	1.30	(1.02, 1.64)	0.031	1.32	(1.03, 1.69)	0.027
No education	1271	34.9	1.49	(1.23, 1.81)	<0.0001	1.31	(1.05, 1.63)	0.018
Paternal education								
Secondary and above	826	30.6	1.00					
Primary	307	33.1	1.12	(0.92, 1.37)	0.246			
No education	706	35.2	1.23	(1.05, 1.44)	0.009			
Parental occupation								
Mother without a job outside the home and father employed	2799	68.3	1.00					
Mother and father both employed	640	65.2	1.15	(0.97, 1.38)	0.115			
Father unemployed	104	59.4	1.47	(1.05, 2.07)	0.025			
Household wealth index								
Richest	268	26.2	1.00					
Richer	336	31.9	1.32	(1.05, 1.67)	0.017			
Middle	355	32.6	1.36	(1.07, 1.74)	0.013			
Poorer	397	33.3	1.41	(1.11, 1.78)	0.004			
Poorest	487	38.0	1.73	(1.36, 2.19)	<0.0001			
Fuel used for cooking								
Biomass energy	1357	34.6	1.00			1.00		
Natural gas/electricity	402	27.8	0.73	(0.61, 0.87)	<0.0001	0.78	(0.65, 0.94)	0.009
Maternal and newborn characteristics								
Maternal age at childbirth								
20–29 years	918	30.8	1.00					
Less than 20 years	871	35.1	1.21	(1.06, 1.39)	0.006			
30 and more	53	29.3	0.93	(0.65, 1.33)	0.687			
Baby's gender								
Male	947	31.1	1.00			1.00		
Female	894	34.5	1.17	(1.03, 1.33)	0.017	1.15	(1.00, 1.32)	0.049
Outcome of pregnancy								
Singleton birth	3771	67.6				1.00		
Multiple births	27	45.8	2.46	(1.41, 4.31)	0.002	2.34	(1.33, 4.13)	0.003
Birth rank								
2nd or 3rd birth rank	568	29.07	1.00			1.00		
1st birth rank	343	35.7	1.31	(1.09, 1.58)	0.004	1.318	(1.07, 1.60)	0.009
≥4th birth rank	931	33.6	1.20	(1.04, 1.38)	0.011	0.99	(0.84, 1.17)	0.935
Desire for pregnancy								
Wanted then	1297	31.6				1.00		
Wanted later	258	34.8	1.16	(0.95, 1.40)	0.147	1.17	(0.95, 1.45)	0.137
Wanted no more	283	36.3	1.24	(1.03, 1.49)	0.026	1.34	(1.08, 1.67)	0.007
Any antenatal services used								
No	681	34.6	1.00					
Yes	1159	31.6	0.87	(0.76, 1.01)	0.066			

Six hundred two missing values were excluded from the analyses. CI, confidence interval; OR, odds ratio. *Model was adjusted for community level, socio-economic status, maternal and newborn characteristics, and antenatal services variables. [†]Weighting was applied to compensate for the multistage cluster sampling design.

Table 6. Effect of iron–folic acid supplementation on birth size in Pakistan: Unadjusted and adjusted odds ratio using multivariate logistic regression analyses

Variables	Smaller than average birth size		Unadjusted			Adjusted*		
	<i>n</i> [†]	% [†]	OR	95% CI	<i>P</i>	OR	95% CI	<i>P</i>
Any IFA supplementation								
No	1121	35.3	1.00			1.00		
Yes	719	29.3	0.76	(0.66, 0.87)	<0.0001	0.82	(0.71, 0.96)	0.013
Timing of start of IFA supplements								
No IFA	1121	35.3	1.00			1.00		
First trimester	322	27.6	0.70	(0.58, 0.84)	<0.0001	0.81	(0.66, 0.99)	0.042
Second/third trimester	311	31.4	0.84	(0.71, 1.00)	0.051	0.88	(0.72, 1.06)	0.186
IFA with other ANC service								
No IFA and no ANC	608	35.8	1.00			1.00		
No IFA but other ANC	513	34.7	0.95	(0.81, 1.13)	0.574	1.01	(0.84, 1.21)	0.955
IFA with or without any ANC	718	29.3	0.74	(0.63, 0.88)	0.001	0.82	(0.68, 0.99)	0.042
Combination of IFA with fuel used for cooking								
No IFA supplementation and biomass energy	916	36.4	1.00			1.00		
No IFA supplementation and natural gas/electricity	152	29.6	0.73	(0.57, 0.94)	0.014	0.77	(0.60, 0.99)	0.043
Any IFA supplementation and biomass energy	441	31.3	0.80	(0.67, 0.95)	0.011	0.81	(0.67, 0.97)	0.023
Any IFA supplementation with natural gas/electricity	249	26.7	0.64	(0.51, 0.79)	<0.0001	0.67	(0.53, 0.85)	0.001

Six hundred two missing values were not included in the analysis. ANC, antenatal care; CI, confidence interval; IFA, iron–folic acid; OR, odds ratio.

*Adjustment for other potential confounders such as community level, socio-economic status, maternal and newborn characteristics, and antenatal care services variables were performed for all models. [†]Weighting was applied to compensate for the multistage cluster sampling design.

Although birthweight was reported in only 11% of the live births in PDHS 2006–2007, our point estimates showed a progressively increasing magnitude of the protective effect of IFA supplementation with decreasing cut-off points for LBW. The greatest magnitude of the protective effect on LBW (although non-significant) was found in infants with birthweight <1500 g (60%) after adjustment for other confounders (Fig. 1).

Our PAR estimates showed that 11% (PAR: 0.11, 95% CI: 0.01, 0.20) of babies with smaller than average birth size were attributed to non-use of antenatal IFA supplements. With universal coverage of IFA supplements, each year in Pakistan 112 000 newborns could be prevented from having smaller than average birth size.

Discussion

Main findings and their significance

We found that the odds of having a newborn of smaller than average birth size was significantly

reduced by 18% in mothers who used any IFA supplements during their pregnancy compared with those who never used supplements after adjustment for other potential confounders. Almost similar protective effect of any IFA supplementation (16%) was also found on LBW (<2500 g) in a subsample analysis, although it was not statistically significant. However, most of the women who reported birthweight of the most recent live birth 5 years prior to the survey belonged to higher socio-economic status in the PDHS 2006–2007, which suggests the need of antenatal IFA supplements to all pregnant women in Pakistan. We also found that the odds of having a newborn of smaller than average birth size was only significantly reduced in those women who started their IFA supplements in the first trimester of their pregnancy. Further, we found no protective effect of using antenatal services without using IFA supplements on the risk of having a newborn of smaller than average birth size. The current study is the first study from Pakistan to report an association between antenatal IFA supplementation and reduced risk of having a newborn of less than average birth size, and LBW, using a

Fig. 1. Effect of iron–folic acid supplementation on birthweight in Pakistan: aOR using multivariate logistic regression analyses. Fifty-five missing values were excluded from the analyses. Adjustment for other potential confounders such as community level, socio-economic status, maternal and newborn characteristics, and antenatal care services variables were performed for all models. All models were also adjusted for reported birthweight based on either maternal recall or written record. *Weighting was applied to compensate for the multistage cluster sampling design. Chi-square test for trends $P < 0.0001$. aOR, adjusted odds ratio; CI, confidence interval; IFA, iron–folic acid.

nationally representative sample. Our findings are likely to play a key part in modifying the current implementation policy of the IFA supplementation programmes in low- and middle-income countries. Importantly, our findings support an early start of antenatal IFA supplementation (in the first trimester) due to significant reduction in the risk of having less than average birth size. Supporting programmes to start supplementation earlier will help low- and middle-income countries to reduce the incidence of LBW and improve the newborn survival to achieve their MDG4 targets.

Comparison with other studies

Our study findings are consistent with a recently published meta-analysis of Randomized Controlled Trials

(RCTs) and observational studies that reported a significant reduction by 19% in the risk of LBW with maternal use of iron supplements compared with controls (Haider *et al.* 2013). An earlier meta-analysis of RCTs found significant 20% reduction in the prevalence of LBW in women who used iron supplements compared with controls (Imdad & Bhutta 2012). A Cochrane review found that maternal use of iron supplements during pregnancy significantly reduced the risk of LBW by 19% compared with controls (Pena-Rosas *et al.* 2012).

Biological mechanism

Recent literature has explained plausible biological mechanisms for the effect of IFA supplements on birthweight. It has been identified that the placenta

plays a central role in the transfer of iron from maternal stores to fetus (McArdle *et al.* 2011; Lipinski *et al.* 2013). Fetal growth requires constant delivery of iron, and therefore, the requirement of iron must be matched by the transport of maternal iron across the placenta (Bastin *et al.* 2006; Lipinski *et al.* 2013). Animal models indicate that the maintenance of adequate iron levels in fetal tissues (including hepatic iron stores) is the highest priority in the hierarchy of iron delivery during pregnancy (Gambling *et al.* 2009; McArdle *et al.* 2011). Therefore, maternal IFA supplementation could help in fetal growth and development throughout pregnancy.

Impact on reduction in prevalence of LBW babies

We calculated the PAR to evaluate the impact of antenatal IFA supplementation on the risk of having a newborn of smaller than average birth size in Pakistan. We found that with universal coverage of IFA supplements, 112 000 smaller than average size live births could be prevented each year in Pakistan. Like most low- and middle-income countries, Pakistan has had for a long time a policy of universal, daily IFA supplementation of pregnant women starting at the beginning of the second trimester of pregnancy and continuing through 45 days post-partum [National Institute of Population Studies (NIPS) [Pakistan] & Macro International Inc 2008]. However, the current coverage of IFA supplements is low (43%) [National Institute of Population Studies (NIPS) [Pakistan] & Macro International Inc 2008] and the lowest in South Asia [International Institute for Population Sciences (IIPS) & Macro International 2007; National Institute of Population Research and Training (NIPORT) *et al.* 2009; Ministry of Health and Population (MOHP) [Nepal] *et al.* 2012]. There is a need to strengthen the IFA supplementation programmes in Pakistan. As an example, Nepal has strengthened its IFA supplementation programme at district level during the last decade (Pokharel *et al.* 2011). Consequently, the coverage of IFA supplementation in Nepal has increased from 23% in 2001 to 80% in 2011 [Ministry of Health and Population (MOHP) [Nepal] *et al.* 2012].

Strengths and limitations

The major strength of our study was the use of a nationally representative sample of Pakistan with a high response rate (95%). Further, the maternal perception of birth size showed a close correspondence with the recorded birthweight in our sample. Although birthweight was recorded for a small percentage of live births in our sample (11%), the subsample analyses found almost similar, but non-significant, protective effect of the antenatal IFA supplementation on LBW.

One of the study limitations was the absence in the PDHS 2006–2007 of some important factors, such as maternal anthropometric measurements, genetic factors and smoking status, which could have been associated with birth size and birthweight. With our model building approach, there is a chance of missing interaction among some explanatory variables entered and eliminated at different stages of model building. A few variables like parental occupation that represented the employment status within the last 12 months preceding the survey were not infant specific because these only presented the most recent conditions. Another limitation was that birthweight was recorded in only 11% of live births and it could not be considered as a nationally representative sample because fewer rural women reported birthweight compared with urban women in the survey. These limitations are unlikely to have had an important effect on the validity of our findings.

To conclude, we found that the use of any IFA supplements during pregnancy reduced the risk of having a newborn of smaller than average birth size and LBW in Pakistan. The extent of the protective effect of the IFA supplements on the odds of newborns of smaller than average birth size was greater when the supplements were started in the first trimester of pregnancy. Therefore, there is a need to modify and strengthen the current IFA supplementation programmes in low- and middle-income countries to increase coverage, improve compliance and encourage women to start supplements as early as possible during their pregnancy to reduce LBW. Such adjustments to IFA supplementation programmes will, through reduced LBW, help improve neonatal

survival and contribute to achieving the MDG4 targets.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Contributions

YBN designed the study, conducted the analyses and prepared the manuscript. MJM provided advice about the data analyses and reviewed the manuscript. All authors read and approved the manuscript.

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