Antenatal Micronutrient Supplementation Relationship with Children's Weight and Height from Birth up to the Age of 18 Months

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Abstract

Background: Maternal nutritional is the most important environmental factor influencing pregnancy outcome. While studies showed association between maternal iron-micronutrient deficiencies with pregnancy outcome, data examining impact of micronutrient supplementation on growth rate beyond birth are sparse. Present study examined the relationship between iron and multivitamins supplementation on growth rate of babies up to age of 18 month.
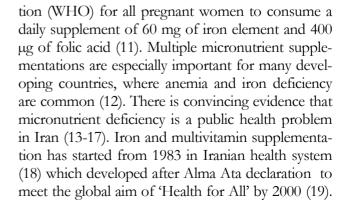
Methods: This study was a statistical analysis on data recorded through a routine procedure in health houses from 1994 to 2007. Subjects were selected by a two-stage randomization method and required data extracted from the records. Analyses were performed using STATA 10 software.

Results: Data was collected for 3835 pairs of mother-baby. Mothers received 61.7±5.4 and 115.6±53.8 multivitamins and iron tablets, respectively. Analyses showed significant relationship between children's weight and height at birth with iron supplementation and children's height at 6, 12 and 18 month with multivitamins supplementation.

Conclusions: Mechanisms of these effects are unclear but it is safe to suggest supplementation during pregnancy is necessary.

Keywords: Iron, Multivitamin supplementation, Intrauterine growth, Neonate growth, Pregnancy

Introduction

Maternal nutritional status is probably the most important environmental factor-influencing outcome of a pregnancy (1-4). Poor maternal multiple micronutrient status has been associated with preterm births (3), low birth weight (5), intrauterine growth retardation (6), increased prenatal mortality (7), smaller head circumference, shorter gestational length (8), birth defects such as neural tube defects (9) and anemia (10) in new-born. In order to prevent these, multiple micronutrient supplementations is strongly recommended by World Health Organiza-tion (WHO) for all pregnant women to consume a daily supplement of 60 mg of iron element and 400 µg of folic acid (11). Multiple micronutrient supplementations are especially important for many developing countries, where anemia and iron deficiency are common (12). There is convincing evidence that micronutrient deficiency is a public health problem in Iran (13-17). Iron and multivitamin supplementation has started from 1983 in Iranian health system (18) which developed after Alma Ata declaration to meet the global aim of 'Health for All' by 2000 (19).

Nowadays there are more than 17000 health houses in rural aria of Iran (15).

These houses, staffing by community health workers, which are responsible for maternal, child health care and other essential services (20). In this care system, all information of the care during pregnancy and after birth of child until school age is documented. Each pregnant woman receives iron sulfate tablets from fourth month of pregnancy until third months after birth of her child. The recommended dose is 1 tablet 4. mg iron element) per day which is g monthly interval. Multivitamins tablet vitamins A, B_1, B_2, B_6, B_{12}, C, D_3, E, and 400-μg folic acid are also given These tablets are given free of charg birth of child, newborns are checked pattern (height and weight) (20). Al and multivitamins supplementation for all pregnant women, but some mo benefit from this program completely various reasons such as late referral tions side effects. Despite relatively l 5. of information on effects of iron or tional supplementation on many aspe er and newborns health, the data ex impact of such interventions beyo sparse (21). Furthermore, little is know effects of the employed process of s tions on newborns lives in Iran.

In the present study, effect of iron an mins supplementation on the growth bies from birth up to the age of 18 examined.

Materials and Methods

The study is a statistical analysis on data recorded through a routine procedure over a 13 year period from 1994 to 2007. For this aim, 20 villages in rural area of Tabriz in East Azerbaijan, Iran were selected randomly from those with active rural health house. The selected population had a less variability economically and socially (based on health and development indicators and research team opinions), and therefore comparing effects of important factors such as iron and multivita-

mins supplementation on growth rate of neonates and infants without some interfering factors was achievable. The inclusion criteria for subjects were:

1.   Women who received care during their pregnancy.
2.   The babies of these women who were alive up to age of 18 months.
3.   Records with complete and extractable information for mother and child.

At the time of sampling there were a total of 28 Health houses in rural area of Tabriz in East Azerbaijan from which 20 villages were selected randomly which covers more than 70% of the available centers. This choice was because of great variability of study variables and to access the representativeness and generalizability of results to the total state. The data was collected for 3835 pairs of mother-child choosing 12% of mothers randomly from eligible cases which cover more than 10% of the total population fulfilling the rule of thumb of 10%.

In addition this sample size is much higher than the sample size suggested by Morgan table (n=384 for this population size, 95% confidence level and 5% marginal error which would be multiplied by 2 (the least value of design effect) results in final n = 768). Furthermore, this sample size is much higher than sample size required in the regression analyses (6 to 10 subjects per variable entered in the model. Among the subjects with all inclusion criteria, 12% was selected from the record system of the health houses by a random method. A 2 stage randomization was used for selection of villages and subjects.

The required data extracted from subjects' records by three trained researchers. Number of iron and multivitamins tablets used by expecting mothers and their age, education, gravid number, month of start of prenatal care and base weight was documented and their relationship was examined with children's height and weight at birth and 6, 12 and 18 months of age. Children's weight and height was measured using standard techniques by trained personnel. All mothers were provided iron and multivitamins tablets throughout the recommended period but because of the variation in subjects compliance (both in tablet taking and health house visit),

the subjects were divided into three groups; subjects who took less than 60 tablets, subjects who took 60-120 tablets and subjects who took more than 120 tablets. This lower rate of tablet use happened despite availability of tablets in health houses. Level of education of women were divided into 6 groups of 1) illiterate, 2) primary school, 3) middle school, 4) high school, 5) high school diploma and 6) university education.

Statistical Analysis

All analyses were performed using STATA 10 Statistical software (Statacorp, College Station, Texas 77845 USA). Multilevel regression analyses were used to assess the relationship of the predictors with weight and height of children at birth, 6 month, 12 month and 18 months' time windows as outcome variables. Time of evaluation and location of health center were considered as temporal and spatial variables and the covariance structure of model was made based on these variables. A compound symmetry covariance structure was used. Parameters were estimated using restricted maximum likelihood (REML) estimation procedure. The explanatory variables entered in each model were mother's education level, mother's age at birth of child, number of pregnancies, care start month, mothers weight at birth of child, mother's multivitamins supplementation levels and iron supplementation levels. Regression coefficients and their standard errors were presented as the effect size of interest (22). *P*-values <0.05 were considered as statistically significant. Current study has been approved by Tabriz University of Medical sciences Ethics committee (Code No 9028).

Results

The data was collected for 3835 pairs of mother-child from March 1994 until April 2007. 51.5% of babies were male. Mean age of mothers was 25.08 ± 5.37 years and mean month of start of prenatal care was 3.20 ± 1.52 months of pregnancy. Mothers mean base weight was 59.3 ± 10.4Kg and mothers received 61.76±52.4 and 115.6±53.8 multivitamins and iron tablets, respectively.

Newborns birth weight and height were 3296.3±473.7 g and 49.6±2.5 cm, respectively. Babies' weight and height at age of 6 months were 7606.8±1002.3g and 64.3±3.8cm, respectively. Babies' weight and height at age of 12 months was 9486.8±1140.1g and 72.6±3.8cm, respectively. Babies' weight and height at age of 18 months was 10620.2±1231.1g and 77.9±4.5cm, respectively (Table 1).

Evaluation of the relationships with children's weight

The results of relationships of the variables with weight are shown in Table 2.

Table 1: Some of demographic data of mothers and children enrolled into the study

Mean Age of Mothers (y)	250.08 ± 5.37	Mean Height of Children at 6 months (cm)	64.3 ± 3.8
Mean Base Weight of Mothers (kg)	59.3 ± 10.4	Mean Weight of Children at 6 months (g)	7606.8 ± 1002.3
Mean Prenatal Care (m)	3.20 ± 1.52	Mean Height of Children at 12 months (cm)	72.6 ± 3.8
Mean Multivitamins Tablet (Consumed by Mother)	61.76 ± 52.4	Mean Weight of Children at 12 months (g)	9486.8 ± 1140.1
Mean Iron Tablet(Consumed by Mother)	115.6 ± 53.8	Mean Height of Children at 18 months (cm)	77.9 ± 4.5
Newborns Birth Weight (g)	3296.3 ± 473.7	Mean Weight of Children at 18 months (g)	10620.2 ± 1231.1
Mean Newborns Birth Height (cm)	49.6 ± 2.5	-	

Table 2: Results of multilevel regression analysis for variables related to the weight of children

Variables	At Birth			6 Months			12 Months			18 Months		
	B	SE	*P*	B	SE	*P*	B	SE	*P*	B	SE	*P*
Education 1[#]	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Education 2	-13.97	21.98	0.525	199.33	47.11	**<0.001**	90.17	54.17	**0.096**	192.95	94.57	**0.041**
Education 3	-48.78	22.71	0.032	175.37	48.52	**<0.001**	91.18	55.78	0.102	263.14	103.08	**0.011**
Education 4	0.28	36.01	0.994	223.18	76.46	**0.004**	202.94	88.78	0.022	399.57	144.50	**0.006**
Education 5	20.40	94.76	0.830	-65.94	197.22	0.738	-101.33	237.64	0.670	10.31	415.85	0.980
Education 6	40.76	232.80	0.861	56.30	483.79	0.907	85.50	560.45	0.879	1331.37	1215.10	0.273
Mother's age at birth	-0.90	1.97	0.648	-3.22	4.18	0.440	-5.92	4.83	0.220	-14.22	7.52	**0.059**
Pregnancy Number	22.94	6.29	**<0.001**	-1.97	13.49	0.884	-6.35	15.55	0.683	28.60	29.85	0.338
Care Starts month	-10.69	6.06	0.078	-13.21	13.48	0.327	-6.79	15.00	0.651	-47.36	24.63	**0.055**
Mother's Weight	6.68	0.80	**<0.001**	18.24	1.68	**<0.001**	19.70	1.95	**<0.001**	22.59	3.03	**<0.001**
Not using Multivitamin[#]	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Using 1-60 Multivitamins tablet	22.77	19.88	0.252	67.95	42.77	0.112	32.95	49.27	0.504	48.41	90.73	0.594
Using 61 – 120 Multivitamins tablet	-6.20	23.65	0.793	16.10	50.47	0.750	-98.54	58.10	**0.090**	21.49	100.74	0.831
Using >120 Multivitamins tablet	-49.83	32.70	0.127	37.86	69.13	0.584	-102.72	79.70	0.197	96.82	130.40	0.458
Not using Ferrous [#]	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Using 1-60 Ferrous tablet	47.98	35.95	0.182	-27.45	76.47	0.720	-127.93	89.35	0.152	-123.57	145.50	0.396
Using 61–120 Ferrous tablet	37.60	34.57	0.277	22.52	73.59	0.760	-6.62	85.92	0.939	15.88	142.12	0.911
Using >120 Ferrous tablet	92.62	35.49	**0.009**	-12.05	75.58	0.873	10.20	88.08	0.908	5.76	147.02	0.969

 # : Reference Category   **B: Regression Coefficient**   **SE: Standard Error**

Results at birth

In this time window, pregnancy number, mothers weight and iron supplementation level showed significant relationship with weight (*P<0.05*). Analyzing results in this time window showed that one unit increase in pregnancy number and one kilogram increase in mothers weight increased weight of children by 22.9g and 6.7g, respectively. Furthermore, using more than 120 iron tablets by mothers increased the weight of children by 92.6g compare to those children whose mothers did not used this supplement. Although, the relationship between mothers age at birth and care start month with children's weight failed to reach a significant level, for each unit increase in mother's age at birth there was an average drop of 14.2g in children's weight and with each month of delay in starting the care, there was an average of 47.4g decline in weight.

Results for 6 months

At age of 6 months, significant relationships were observed between children's weight with mother's education level and mothers weight (*P<0.05*). Analyzing results in this time window showed that one-kilogram increase in mothers' weight caused an 18.2g increase in weight of children. Furthermore, children's weight in-group of mothers with education levels of 2, 3 and 4 was 199.3g, 175.4g

and 223.2g heavier than those with mothers with education level of 1.

Results for 12 months

At age of 12 months, significant relationships between children's weight were observed only with mothers weight (*P<0.05*). Analyzing results showed that one kilogram increase in mothers' weight caused an average 19.7 g increase in children weight. Based on results, mothers with education levels of 2 had heavier children than those with education level of 1 (an average of 90.2g). Unexpectedly, using 61 – 120 multivitamins tablets during pregnancy caused a 98.5g reduction in children's weight compare to those who did not used multivitamin.

Results for 18 months

At this age, significant relationships was observed between children's weight with mothers education level and weight (*P<0.05*). The results showed that one-kilogram increase in mothers' weight caused an average increase of 22.6g in weight of children at this age.

Evaluation of the relationships with children's height

The results of relationships of the variables with height are shown in the Table 3.

Table 3: Results of multilevel regression analysis for variables related to the height of children

Variables	At Birth			6 Months			12 Months			18 Months		
	B	SE	P	B	SE	P	B	SE	P	B	SE	P
Education 1#	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Education 2	0.01	0.12	0.917	0.55	0.19	0.004	0.32	0.19	0.089	0.51	0.36	0.160
Education 3	-0.03	0.13	0.812	0.10	0.19	0.606	0.18	0.19	0.333	0.70	0.39	0.071
Education 4	-0.11	0.20	0.588	0.42	0.30	0.170	0.13	0.30	0.654	1.31	0.53	0.014
Education 5	-0.45	0.54	0.410	-0.44	0.79	0.574	0.46	0.79	0.565	-1.12	1.54	0.469
Education 6	-0.88	1.41	0.535	3.88	2.15	0.072	4.34	2.11	0.040	----	----	----
Mother's age at birth	0.00	0.01	0.733	-0.04	0.02	0.015	-0.02	0.02	0.174	0.07	0.11	0.519
Pregnancy Number	0.09	0.03	0.010	0.08	0.05	0.147	0.07	0.05	0.200	-0.17	0.09	0.057
Care Starts month	-0.07	0.03	0.022	0.05	0.05	0.379	0.03	0.05	0.588	0.05	0.01	<0.001
Mother's Weight	0.03	0.00	<0.001	0.04	0.01	<0.001	0.04	0.01	<0.001	----	----	----
Not using Multivitamin#	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Using 1-60 Multivitamins tablet	-0.04	0.11	0.699	0.35	0.17	0.044	0.35	0.17	0.038	1.10	0.35	0.001
Using 61 – 120 Multivitamins tablet	-0.08	0.13	0.516	0.74	0.20	<0.001	0.38	0.20	0.060	0.61	0.38	0.111
Using >120 Multivitamins tablet	-0.08	0.17	0.649	0.78	0.28	0.005	1.01	0.28	<0.001	0.88	0.49	0.071
Not using Ferrous #	0.00	----	----	0.00	----	----	0.00	----	----	0.00	----	----
Using 1-60 Ferrous tablet	0.20	0.20	0.297	-0.41	0.30	0.175	-0.49	0.30	0.103	-1.67	0.53	0.002
Using 61 – 120 Ferrous tablet	0.24	0.19	0.194	-0.29	0.29	0.308	-0.51	0.29	0.076	-1.42	0.52	0.006
Using >120 Ferrous tablet	0.49	0.19	0.010	-0.03	0.30	0.908	-0.28	0.29	0.338	-1.27	0.54	0.019

: Reference Category   B: Regression Coefficient   SE: Standard Error

Results at birth

There was a significant relationship between gravid number, mothers' weight, care starts month and iron supplementation level with newborn height ($P<0.05$). Results of data analysis showed that one unit increase in gravid number, mothers' weight and iron supplementation level caused an average 0.09, 0.03 and 0.49cm increase in newborns height. On the other hand, one unit increase in care starts month decreased height of children by an average of 0.07cm.

Results for 6 months

At six months of age, there was a significant relationship between children height with mothers education level, age and weight and multivitamins supplementation level ($P<0.05$). The results at this time window showed that one-kilogram increase in mothers' weight during pregnancy caused an average of 0.04 cm increase in children height. A greater increase was seen in height of children whose mothers had taken more than 120 multivitamins tablets (0.78cm) but the greatest increase was seen in children of mothers with education level of 6, which was equal to 3.88 cm.

Results for 12 months

At the age of 12 month, a significant relationship was between children's height and mothers weight and multivitamins supplementation level ($P<0.05$). Furthermore, analysis showed that for each kilogram increase in mothers' weight, an increase of 0.04 cm was observed in children height. The highest increase in children's height was observed in group of mothers who took more than 120 multivitamins tablets during pregnancy.

Results for 18 months

At the age of 18 month, there was a significant relationship between children's height and mothers education level, multivitamins and iron supplementation and gravid number ($P<0.05$). Interestingly, the relationship between children's height and iron supplementation level during pregnancy was a significant but an inverse one.

Discussion

Many studies and randomized clinical trials are focusing on iron and micronutrient supplementation during pregnancy and its effects on pregnancy outcomes, infant development (1,23-27) and relationship between iron deficiency anemia and neonates low weight are shown in many studies (28,29). Despite this, evidence for reduced risk of low birth weight and preterm birth with iron supplementation is weak (30) and there is no study on effects of folic acid on birth weight or gestational age (31), but a study on 15378 women showed that supplementation with multivitamins significantly reduced number of low birth weight newborns and mothers anemia (23).

In present study, iron supplementation during pregnancy caused a raise in weight and height of children at birth and mothers who took more than 120 iron sulfate tablets had newborns heavier and taller than those who did not take any iron supplements. Multivitamins supplementation was not effective in weight or height of newborns. At age of 6 months, children's height was significantly related with multivitamins supplementation. Interestingly similar relationship was also seen at 12 months and 18 months of age but the relationship at age of 18 months was weaker. The height of children at age of 6 to 18 months had no relationship with iron intake of mother during pregnancy but it was related to some or all elements of multivitamins tablets. Finding of current study shows that level of iron supplementation by mother has a significant relationship with weight at birth but not at other ages. Multivitamins supplementation showed no effects on weight at any of measuring points. This result was not in agreement with Vaidya et al. clinical trial, in which children born to mothers under supplementation (vitamins and minerals) were 204 g heavier than those who only received iron and folic acid (32).

Results of this study showed a significant relationship between children's weight and height at birth with iron supplementation and children's height at 6, 12 and 18 month with multivitamins supplementation. Vaidya et al. study, showed no rela-

tionship between height at age of 2.5 years with iron and folic acid usage or micronutrients usage (32). Vaidya study was an interventional randomized clinical trial with 2 groups but our study was a retrospective study and because of supplementations provided for decades for teenage girls or during previous pregnancies, the present subjects might have had higher storage level of iron. The Hemoglobin level was available in records of 1861 subjects, its mean was 12.90 ± 1.10 g/dL, and body mass index of all subjects was 25.09 ± 4.75 kg/m^2.

In recent years, there have been many studies in the world and especially in developing countries aiming chronic diseases and their origin and prognosis. One previous study showed that supplementations with folic acid or iron plus folic acid reduced renal disorders and to some extent metabolic syndrome in children age 6-8 years (27). In another study, it was shown that there was no relationship between intelligent quiescent at age of 4 years and iron supplementation, while the same study failed to show a relationship between mothers' health and supplementation during pregnancy (25). In another clinical trial, researchers showed that iron status in children aged 6 months and 4 years, did not correlate with supplementation of their nutritionally competent pregnant mothers (26). In general, limited studies showed iron supplementation has weak effects on various aspects of life or health during childhood. These results were in agreement with current study.

In another study, it was shown that multivitamins supplementation caused an increase in birth weight and head circumstance (8) while another study showed multi micronutrient supplements in mothers with low BMI was more effective (24). In our study, there was a significant relationship between height grow rate at 6, 12 and 18 month with multivitamins supplementation, but mechanism behind this relation is unclear or it is unclear which part of multivitamins was responsible for this effect. It is also unclear what kind of effect co-prescription of iron and multivitamins could have. To answer these questions, there is a need for a more extended and accurate studies.

Suggestion

Designing and performing long- term studies on effects of iron or multivitamins supplementation in Iran is necessary. Designing of such studies is requiring noticing all relevant factors in iron or multivitamins supplementation side and growth monitoring side. This is possible because of high potential of Iranian health system especially in health houses of rural area.

Limitation of the study

The limitation of the study was the exclusion of deceased children younger than 18 months of age. It was possible that among other reasons lack of supplementation have acted as an important factor in child death. Furthermore, we did not have sufficient information about (preterm births, intrauterine growth retardation, smaller head circumference, shorter gestational length, and birth defects) in health houses; therefore, we focused on weight and height of infants.

Conclusion

Significant effects of supplementation with different amount of multivitamins on growth rate are seen here as well as other studies. It is important to emphasis on continues supplementation in the health system and on further studies for recognizing other aspects of current health systems.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

Acknowledgement

sity of Medical Sciences (Tabriz - Iran). The authors declare that there is no conflict of interest.

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