Maternal knowledge and use of folic acid among Saudi females

Ali A. Al-Akhfash, MD, Abdelmagid M. Abdulla, MD, Amani M. Osman, MD, Julnar I. Abdulgafar, MD, Abdulrahman A. Almesned, MD.

ABSTRACT

الأهداف: دراسة معرفة أهمية حمض الفوليك، واستخداماته الحالية، ووقت استخدمه لدى النساء الحوامل.

الطريقة: أجريت دراسة استعراضية بشكل عشوائي على النساء اللواتي تتراوح أعمارهن بين 45-18 عام في عيادة النساء والولادة في مستشفى الولادة والأطفال، القسيم، المملكة العربية السعودية خلال الفترة من يناير حتى نوفمبر 2012م. تم استبيان 1250 امرأة، وأبدت 1000 (80.8%) منهن موافقتهن في المشاركة في الدراسة. يتكون الاستبيان من 17 بند. وتم تحليل النتائج باستخدام التحليل المتعدد والأحادي.

النتائج: تبين أن 88.4% من السيدات على علم بحمض الفوليك لكن فقط 4.4% منهن يتناولن حمض الفوليك قبل الحمل. 20.4% من النساء المتعلمات أعلى استخداماً للفيتامين خلال الأشهر الثلاثة الأولى بالمقارنة مع 5٪ فقط من النساء الأميات. وأظهر التحليل أحادي المتغير والمتغيرات المتعددة أن المستوى التعليمي له ارتباط كبير مع الوعي وكذلك استخدام فيتامين حمض الفوليك. بين في الاستبيان أن48 سيدة (4.8%) لديهن تاريخ مرضى بولادة أو وجود طفل لديه تشوهات خلقية. 8.3% فقط منهن يستخدمن حمض الفوليك قبل الحمل.

خاتمة: على الرغم من الوعى من وجود بحمض الفوليك، %4.4 من النساء فقط يستخدمنه في الفترة ما قبل الحمل. يؤدي ارتفاع المستوى التعليمي إلى المزيد من المعرفة وكذلك استخدام حمض الفوليك المستوى الضعيف من استخدام حمض الفوليك في الوقت المناسب يتطلب زيادة التوعية بأهمية ذلك وقد يتطلب دعم الغذاء بحمض الفوليك.

Objectives: To explore and find out the level of awareness regarding folic acid's (FAs) importance, current use, and timing of administration among pregnant Saudi females.

Methods: This is a cross-sectional study conducted randomly among women aged 18-45 years old, attending the Antenatal and Gynecology Clinics at the Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia from January to November 2012. A total of 1250 subjects were approached, and 1000 women expressed their verbal consent to participate. The questionnaire consisted of 17 items, and results were analyzed using univariate and multivariate analysis.

Results: A total of 88.4% of women were aware of FA. However, only 4.4% of them took FA before pregnancy. Compared to highly educated women (20.4%), only 5% of illiterate women use FA during the first trimester of their pregnancy. Univariate and multivariate analysis showed that educational level had a significant association with FA awareness and use (p=0.001; odds ratio: 0.000; 95% confidence interval: 1.001 to 1.080). Most women recall hearing of FA from their doctors. Only 48 women reported a history of a previous child with congenital anomalies, and 4 of them (8.3%) of them used FA before pregnancy.

Conclusion: We found that only 4.4% of the studied women use FA in their preconceptional period. The higher the educational level, the more the knowledge, and frequent use of FA. Poor level of awareness among lower educated woman requires medical authorities to broadcast the importance of FA, and there may be a need to fortify food with FA.

Saudi Med J 2013; Vol. 34 (11): 1173-1178

From the Departments of Pediatric Cardiology (Al-Akhfash, Osman, Abdulgafar, Almesned), Obstetrics and Gynecology (Abdulla), Prince Sultan Cardiac Center, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia.

Received 9th July 2013. Accepted 16th September 2013.

Address correspondence and reprint request to: Dr. Abdulrahman A. Almesned, Pediatric Cardiology Department, PO Box 896, Prince Sultan Cardiac Center, Maternity and Children's Hospital, Buraidah, Al-Qassim 51421, Kingdom of Saudi Arabia. Tel. +966 555139090. E-mail: almesnid@yahoo.com

 \mathbf{F} olic acid (FA) is one of the B complex vitamins, and is now recognized as a major component of the preconceptional care of women in the reproductive age group. A deficiency of FA can lead to neural tube defects (NTDs) in the fetus, and megaloblastic anemia in the mother. Spina bifida and anencephaly (the most common NTDs) are serious birth defects that occur early in pregnancy, often before a woman realizes that she is pregnant. Important studies show that intake of the B vitamin folic acid reduces the incidence of NTDs by 50-70% when taken before conception and during the first trimester of pregnancy. 1-3 Many studies have shown that FA supplementation in pregnancy is effective in preventing these births defects. 4-6 Folic acid supplementation, 3 months prior to conception until 12 weeks gestation has been shown to decrease both the occurrence and recurrence of NTDs.7 Moreover, it was found that women who took 4 mg of FA daily during the preconceptional period in a subsequent pregnancy had a 72% reduction in the risk of having an affected fetus or infant.7 Consequently, routine supplementation of FA has been recommended by many health authorities including the World Health Organization (WHO) and the Centre for Disease Control (CDC).8,9 There are reported evidence indicating that folate deficiency is not only associated with macrocytic megaloblastic anemia, which is widespread especially in pregnant women, but also with NTD's in high-risk population groups, elevated plasma homocysteine levels, and thus increased risk of coronary heart disease and stroke, and various cancers, particularly of the colon. Due to these concerns, the WHO expert committee on the use of essential drugs (1997) recommend an increase of the folate content in the iron (Fe)/folate tablet from 250-400 mg, which translates into a more appropriately dosed iron/folate tablet (60 mg Fe/400 mg folate) for supplementing women of childbearing age. 10 In the Kingdom of Saudi Arabia (KSA), there was a geographical variation in the incidence of NTDS. In Southwestern KSA,¹¹ the incidence was 0.82/1000 births, and in the Asir region it was 0.78/1000 births.¹² Another report from KSA has shown that there was a decline in the incidence of NTDs from 1.9/1000 live births (1997-2000) to 0.76/1000 live births (2001-2005) after fortifications of flour with FA.13 In Qassim region, the incidence was highest among the reported regions in KSA (6.9/1000

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

population in 1991).¹⁴ Knowledge and awareness on the value of FA is important to prevent these births defects. However, despite the recommendations and national campaigns, preconceptional intake of additional FA is still low in many countries. In KSA, all pregnant women are supplied with FA tablets free of charge in antenatal visits. There were 2 studies performed in KSA among female college students regarding FA awareness, ^{15,16} however in the general population, no study was carried out to include all sectors of the community. Therefore, the aim of the present study is to explore the maternal knowledge and FA intake among Saudi women at the reproductive age including the different sociodemographic characteristics of the community.

Methods. In this cross-sectional study, data were collected from women attending the Antenatal and Gynecology Clinics at the Maternity and Children Hospital, Buraidah, Al-Qassim, KSA from January to November 2012. The questionnaire was administered to randomly selected women aged 18-45 years old. The study was approved by the research committee of the hospital. To determine the sample size required, we assumed that the level of FA awareness among Saudi women is equal, or higher than what was reported in the neighboring countries, ¹⁷ allowing an error of 3%, level of significance of 1 (type 1 error), and confidence interval of 95%. A computer program indicated that a sample size of 1066 subjects is required to achieve the objectives of our study. The sample was selected by simple random sampling among women who visited the antenatal clinics. Two resident physicians were instructed to interview and complete the questionnaire after adequate training. Verbal consent and confidentiality were obtained prior to survey. A total of 1250 subjects were approached, and a total of 1000 (80.8%) women agreed to participate in the study. The questionnaire consists of 17 items and designed by researchers to cover the knowledge and use of FA supplements, source of knowledge regarding FA, the time of intake in relation to pregnancy trimesters, diet rich in FA, and potential benefits of taking FA during pregnancy. Additionally, other variables were included, such as maternal age, parity, previous obstetric history, previous child with congenital anomalies, and type of malformations, and level of education.

The Statistical Package for Social Sciences version 20 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. To examine the association of awareness and how other sociodemographic and obstetric characteristics predict the level of awareness regarding intake of FA supplement, we used both univariate and

multivariate logistic regression analyses. Chi-square analysis was performed to test the differences between the categorical variables. The student's t-test (2-tailed) was used to examine the significance of difference between the means of numerical variables. In multivariate analysis, all independent variables were added to the model simultaneously. The results of these analyses are presented as odds ratios (OR) and 95% confidence intervals (CI). A p<0.05 was considered statistically significant.

Results. The important characteristics of the interviewed women are represented in Table 1. The most common age group interviewed were those between 26-30 years of age (28%). Approximately 31% were not pregnant at the time of interview. Most of the interviewed women have one to 3 pregnancies (52.7%), and 30% of them are university graduates. The association of knowledge and intake of supplementary FA with age and education of the women, as well as with other sociodemographic characteristics was also calculated (Table 2). As high as 88% of the women reported that they had heard regarding FA. Despite these results, few women use it in the preconceptional period and in the first trimester. The higher the educational level, the more women are aware regarding FA, as

Table 1 - Characteristics of the interviewed women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia

Category	n	n (%)	
Age group			
18-25	230	(23.0)	
26-30	282	(28.2)	
31-35	228	(22.8)	
36-40	187	(18.7)	
41-45	73	(7.3)	
Educational level			
Illiterate	132	(23.0)	
Primary	137	(13.7)	
Intermediate	150	(15.0)	
Secondary	250	(25.0)	
University	308	(30.8)	
Postgraduate	23	(2.3)	
Pregnancy status			
Pregnant	693	(69.3)	
No	307	(30.7)	
Parity			
1-3	527	(52.7)	
4-5	256	(25.6)	
6+	217	(21.7)	

Table 2 - Time of folic acid intake in association with age group, educational level, parity, and history of previous anomalous baby in women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia (N=1000).

	Folic acid intake time				Total	
Characteristics	Before pregnancy	First 3 months	After 3 months	Throughout the pregnancy	Before pregnancy and first 3 months	
Age group						
18-25	12	159	27	19	13	230 (23.0)
26-30	17	165	41	40	19	282 (28.2)
31-35	9	120	41	35	23	228 (22.8)
36-40	4	99	56	19	9	187 (18.7)
41-45	2	28	33	6	4	73 (7.3)
Educational level						
Illiterate	1	51	70	9	1	132 (13.2)
Primary	4	72	36	13	12	137 (13.7)
Intermediate	4	87	30	23	6	150 (15.0)
Secondary	12	157	37	34	10	250 (25.0)
University	22	188	24	38	36	308 (30.8)
Postgraduate	1	16	1	2	3	23 (2.3)
Parity						
1-3	33	322	65	67	40	527 (52.7)
4-5	6	154	51	26	19	256 (25.6)
6+	5	95	82	26	9	217 (21.7)
History of previous baby with anomalies						
Yes	4	28	6	6	4	48 (4.8)
No	40	543	192	113	64	952 (95.2)

well as, more frequent use of FA - prior and during pregnancy. Regarding intake of FA, only 4.4% of the studied women take FA prior to pregnancy. A total of 2.3% are those with university graduation and more) against 0.01% of the illiterate women. During the first trimester, 20.4% of highly educated women used FA during the first trimester compared to only 5% of illiterate women. Despite that 88% of the interviewed women were aware of the existence of FA, 53.8% of them are aware that FA prevent fetal anomalies, 31.2% does not know its importance, and 72.9% are not aware

Table 3 - Univariate analysis of the association between some selected sociodemographic characteristics and awareness regarding folic acid of women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia.

Characteristics	Odds ratio	95% confidence interval	P-value
	Odds ratio	93% confidence interval	1-value
Age			
18-25	1.00		
26-30	3.299	0.884-12.315	0.076
31-35	3.157	0.811-12.296	0.097
36-40	4.479	1.133-17.708	0.063
≥41	6.592	1.564-27.776	0.07
Parity			
1-3	1.00		
4-5	1.117	518-2.411	0.778
≥6	1.716	788-3.740	0.174
Educational level			
Illiterate	1.00		
Primary	0.153	1.132-1.232	0.003
Intermediate	0.162	1.037-1.132	0.001
Secondary	0.021	1.049-1.132	0.001
University and more	0	1.001-1.080	0.001

of FA resources. The most common reported sources of information on FA were from the health care service (70.3%), radio and TV (2%), nurses and midwives (0.4%), and internet (7%). Tables 3, 4, and 5 show the univariate and multivariate analyses of the association between sociodemographic characteristics awareness, preconceptional FA intake, and FA intake during the first 3 months of pregnancy. They showed no correlation between FA intake and age group or parity, but there was a significant association between FA intake, as well as timing of intake with educational level (p=0.001). The higher the educational level, the more knowledge and awareness regarding FA, as well as, the more often use of FA in the preconceptional and first trimester period (OR: 0.000; 95% CI: 1.001-1.080). There were 48 of the interviewed women (4.8%) who mentioned that they have a previous child with congenital anomalies. Most of them were aware regarding FA and its use during pregnancy, but only 4 of them (8.3%) used it before pregnancy. Congenital heart disease was the most common congenital anomaly (Table 2 & Table 6).

Discussion. The awareness of folic acid in the current study is 88% when compared to Qatar (53.7%),¹⁸ United Arab Emirates (46.6%),¹⁷ and Lebanon (60%).¹⁹ Despite the existence of scientific evidence on the effectiveness of FA supplementation in the prevention of NTDs, and its recommendation by healthcare authorities, only 4.4% of women in our study took this vitamin properly (starting from the

Table 4 - Univariate and multivariate analysis of folic acid intake preconception with some selected demographic characteristics of women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia.

Variable		Univariate			Multivariate		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	
Age group							
18-25	1.00			1.00			
26-30	1.67	0.68-1.50	0.596	1.02	0.63-2.41	0.57	
31-35	1.34	0.710-2.09	0.495	1.01	0.61-2.01	0.593	
36-40	0.23	0.50-1.46	0.518	0.56	0.45-1.38	0.643	
41-45	0.45	0.70-2.11	0.326	0.65	0.51-2.11	0.712	
Parity							
1-3	1.00			1.00			
1-5	0.87	0.61-1.80	0.619	0.67	0.41-1.55	0.521	
<u>≥</u> 6	0.56	0.46-2.02	0.052	0.79	0.56-1.82	0.66	
Educational level							
Illiterate	1.00			1.00			
Primary	2.89	1.18-4.61	0.001	0.65	0.34-2.81	0.881	
Intermediate	2.10	0.61-3.99	0.41	0.96	0.31-2.01	0.321	
Secondary	1.94	1.81-5.68	0.002	0.78	0.18-1.70	0.48	
University and more	2.76	1.61-5.31	0.004	0.39	0.19-1.75	0.002	

Table 5 - Univariate and multivariate analysis of folic acid intake during the first 3 months of pregnancy with some selected demographic characteristics of women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia.

Variable	Univariate			Multivariate		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Age group		-				
18-25	1.00			1.00		
26-30	0.81	0.51-1.18	0.01	0.84	0.61-1.81	0.7167
31-35	0.51	0.27-0.89	0.01	1.4	0.70-2.06	0.412
36-40	0.81	0.50-0.99	0.91	2.01	0.89-2.10	0.03
41-45	0.62	0.39-1.28	0.78	2.08	0.96-2.10	0.09
Parity						
1-3	1.00			1.00		
1-5	0.8	0.67-0.98	0.02	0.87	0.94-2.01	0.36
≥6	0.31	0.42-0.81	0.03	0.68	0.61-1.98	0.64
Educational level						
Illiterate		1.00		1.00		
Primary	0.72	0.61-3.01	0.494	1.01	0.92-2.71	0.672
Intermediate	1.23	0.92-2.92	0.321	0.62	0.47-2.01	0.601
Secondary	2.21	1.91-4.02	0.01	0.45	0.61-1.01	0.02
University and more	4.12	3.29-7.61	0.02	0.21	0.20-1.92	0.001

Table 6 - Congenital anomalies and timing of administration of folic acid in women included in a study conducted at the Antenatal and Gynecology Clinics, Maternity and Children's Hospital, Al-Qassim, Kingdom of Saudi Arabia (n [%]).

T (1:	Folic acid	Total	
Type of anomalies	Before pregnancy After getting pregnant		
No previous anomalous child	40 (4.0)	911 (91.1)	951 (95.0)
Neural tube defect	1 (0.1)	4 (0.4)	5 (0.5)
Skeletal	0	7 (0.7)	7 (0.7)
Cardiac	0	16 (1.6)	16 (1.6)
Others	3 (0.3)	18 (1.8)	21 (2.1)
Total	44 (4.4)	956 (95.6)	1000 (100)

preconceptional period). Approximately 57% of women in the current study took FA during the first trimester. This finding is comparable to what was reported before regarding the use of FA among pregnant ladies in the developed and developing countries, which was reported to be approximately 20-70%. 18,20

The inadequate intake of FA at the proper time may be due to multiple reasons, the most important is the lack of proper health education, and preconceptional education and planning. Other investigators also reported that women with higher education level knew more regarding FA, as well as using it more often in the preconceptional period.¹⁸ The younger the age, the higher the educational level, and the more sufficient and stable the income, the more the awareness and use of FA among Lebanese women.¹⁹ In a study performed in 2001 in the Asir region regarding risk factors for NTD, they found that only 25% of the 64 mothers who have a child born with NTD were on folate supplementation during the affected pregnancy, and no mother received FA supplementation in the preconceptional period.¹¹

To make sure women that receive sufficient folate, we have to implement educational programs and we may need to carry out folate fortification. Educational programs were the first intervention to be initiated in both the United States and Canada, and this is the intervention currently being used in most countries. In follow-up studies, folate use has been shown to increase among educated women and women of higher socioeconomic status.²¹ Folate fortification is an attempt to increase the daily folate intake for all women of childbearing age through supplementation in the food chain. This has been carried out in both the United States and Canada since 1998.²² The objective has been to obtain an average daily dose of 0.4 mg of folate.²² As folate is an important cofactor in the metabolism of one-carbon molecules and has an important role in DNA synthesis and replication, adequate folate intake is essential. Folate deficiency is associated with high plasma concentrations of homocysteine, which is a potential risk factor for atherosclerosis.²³

Some experts have concerns regarding the noticed transient increase in colorectal cancer risk during the early post FA fortification period.²⁴ The aim of folate fortification is to increase the periconceptional folate concentrations in women of child bearing age.²⁵ As the targeted group for folic acid supplementation is women in the childbearing age, we do not know if it is justifiable to expose the whole community to fortified foods with an uncertain risk associated with this enrichment. Alternative strategies, such as an intervention targeting individuals at high risk, or the addition of folate to oral contraceptives, might be considered, rather than placing the entire nations on folate.

This study was limited as it was carried out in only one hospital in KSA. It may not represent the actual situation in the whole country. We are not fully aware, or have no clear idea regarding food fortification in KSA.

In conclusion, despite the high awareness regarding FA among Saudi women compared to the neighboring countries, minority of them uses it in the preconceptional period. No correlation was found between FA intake and age group and parity, but educational level shows a significant association. The higher the educational level, the more awareness, knowledge, as well as use of FA. Women in the reproductive age group should be advised regarding the benefits of FA supplementation during the preconceptional period using different ways including media (TV and radio), educational, and media campaigns.

Acknowledgment. The authors gratefully acknowledge Mrs. Malica Medali, Secretary, Pediatric Cardiology, Prince Sultan Cardiac Centre, Al Qassim, Kingdom of Saudi Arabia for her assistance in this study.

References

- Wilson RD, Johnson JA, Wyatt P, Allen V, Gagnon A, Langlois S, et al. Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies. *J Obstet Gynaecol Can* 2007; 29: 1003-1026. English, French
- Chen G, Song X, Ji Y, Zhang L, Pei L, Chen J, et al. Prevention of NTDs with periconceptional multivitamin supplementation containing folic acid in China. *Birth Defects Res A Clin Mol Teratol* 2008; 82: 592-596.
- King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. J Nutr 2003; 133 (Suppl 2): S1732-S1736.
- Czeizel AE, Dudás I, Paput L, Bánhidy F. Prevention of neural-tube defects with periconceptional folic acid, methylfolate, or multivitamins? *Ann Nutr Metab* 2011; 58: 263-271.
- Fehr KR, Fehr KD, Protudjer JL. Knowledge and use of folic acid in women of reproductive age. *Can J Diet Pract Res* 2011; 72: 197-200.

- Nasr Hage C, Jalloul M, Sabbah M, Adib SM. Awareness and intake of folic acid for the prevention of neural tube defects among Lebanese women of childbearing age. *Matern Child Health J* 2012; 16: 258-265.
- Blencowe H, Cousens S, Modell B, Lawn J. Folic acid to reduce neonatal mortality from neural tube disorders. *Int J Epidemiol* 2010; 39 (Suppl 1): 110-121.
- 8. Greiner T. Vitamins and minerals for women: recent programs and intervention trials. *Nutr Res Pract* 2011; 5: 3-10.
- Centers for Disease Control and Prevention (CDC). Trends in folic acid supplement intake among women of reproductive age---California, 2002--2006. MMWR Morb Mortal Wkly Rep 2007; 56: 1106-1109.
- World Health Organization. Nutrition for Health and Development. Available from URL: http://www.who.int/ mip2001/files/2231/NHDprogressreport2000
- Asindi A, Al-Shehri A. Neural tube defects in the Asir Region of Saudi Arabia. Ann Saudi Med 2001; 21: 26-29.
- El-Awad Mel-H, Sivasankaran S. Neural tube defects in Southwestern region of Saudi Arabia. *Ann Saudi Med* 1992; 12: 449-452.
- Safdar OY, Al-Dabbagh AA, Abuelieneen WA, Kari JA. Decline in the incidence of neural tube defects after the national fortification of flour (1997-2005). Saudi Med J 2007; 28: 1227-1229.
- Hegazy IS, Al-Beyari TH, Al-Amri AH, Qureshi NA, Abdelgadir MH. Congenital malformations in primary health care in Al-Qassim region. *Ann Saudi Med* 1995; 15: 48-53.
- Al-Mendalawi MD. Folic acid awareness among female college students: neural tube defect prevention. Saudi Med J 2009; 30: 723.
- Kari JA, Bardisi ES, Baitalmal RM, Ageely GA. Folic acid awareness among female college students: neural tube defect prevention. Saudi Med J 2008; 29: 1749-1751.
- Abdulrazzaq YM, Al-Gazali LI, Bener A, Hossein M, Verghese M, Dawodu A, et al. Folic acid awareness and intake survey in the United Arab Emirates. *Reprod Toxicol* 2003; 17: 171-176.
- 18. Bener A, Al Maadid MG, Al-Bast DA, Maternal knowledge, attitude and practice on folic acid intake among Arabian Qatari women. *Reprod Toxicol* 2006; 21: 21-25.
- Nasr Hage C, Jalloul M, Sabbah M, Adib SM. Awareness and intake of folic Acid for the prevention of neural tube defects among Lebanese women of childbearing age. *Matern Child Health* J 2012; 16: 258-265.
- Morin P, De Wals P, St-Cyr-Tribble D, Niyonsenga T, Payette H. Pregnancy planning: a determinant of folic acid supplements use for the primary prevention of neural tube defects. *Can J Public Health* 2002; 93: 259-263.
- Green-Raleigh K, Carter H, Mulinare J, Prue C, Petrini J. Trends in folic Acid awareness and behavior in the United States: the Gallup Organization for the March of Dimes Foundation surveys, 1995-2005. *Matern Child Health J* 2006; 10 (Suppl 5): S177-S182.
- Berry RJ, Bailey L, Mulinare J, Bower C; Folic Acid Working Group. Fortification of flour with folic acid. *Food Nutr Bull* 2010; 31 (Suppl 1): S22-S35.
- McNulty H, Pentieva K, Hoey L, Ward M. Homocysteine, B-vitamins and CVD. *Proc Nutr Soc* 2008; 67: 232-237.
- 24. Zschäbitz S, Cheng TY, Neuhouser ML, Zheng Y, Ray RM, Miller JW, et al. vitamin intakes and incidence of colorectal cancer: results from the Women's Health Initiative Observational Study cohort. *Am J Clin Nutr* 2013; 97: 332-343.
- 25. Eichholzer M, Tonz O, Zimmermann R. Folic acid: a publichealth challenge. *Lancet* 2006; 367: 1352-1361.