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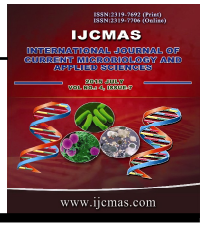

Original Research Article

Adherence to Folic Acid Supplements during Peri-Conceptional Period

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Keywords

Adherence, Folic acid supplement, Knowledge, Peri-conceptional period, Pregnant, Maternal and fetus problems

A B S T R A C T

Daily intake of folic acid supplement by a woman eight weeks before conception and throughout the first twelve weeks of gestation helps protect against a number of the maternal and her fetus problems is one of the most important things to prevent serious birth defects in a baby and to avoid women pregnancy complications and also depression after delivery. It is therefore imperative to assess women adherence during peri-conceptional period to the prescribed folic acid supplement and to determine the factors affecting their adherence to these supplements. Lastly, assessment of their knowledge about folic acid aspects. This descriptive study included 136 women which were planning to be pregnant or they were early pregnant. Questionnaires, pill counts, prescription refill rates, and patient self-reporting were employed for adherence assessment. The mean age was (26.7± 5.8) years. Overall, the parameters analyzed indicated significantly worse adherence to folic acid daily administration. Adherence was satisfactory in 70 (51.47%) and poor in 66 (48.53%). Moreover, the pregnant knowledge about folic acid aspects reflected that most of pregnant women didn't have enough information about folic acid for instance 64.70% didn't know the benefit of folic acid during pregnancy and unfortunately 44.12% didn't know the folic acid regimen. Adherence rate was very low. New strategies addressed to improve drug adherence with folic acid supplements at least two months before conception and for three months during pregnancy.

Introduction

Folic acid is the synthetic and most stable form of folate (a water-soluble B vitamin), its bioavailability is approximately 70% higher than that of folate naturally contained in foods, although there are wide variations depending on the methodology used in the measurement (McNulty and Pentieva, 2004). About 4–5 microgram is excreted daily in the urine. The mean dietary intake of folic acid is about 0.1–0.2 mg per day.

It is reduced in the body to tetrahydrofolate, a coenzyme for many metabolic reactions including DNA synthesis and amino acid conversion. Folic acid supplementation is well tolerated, although gastrointestinal side effects may occur.

Women are especially susceptible to folate deficiency during pregnancy, which is a period of rapid fetal growth, organ

differentiation and high rates of cell division (Tamura and Picciano, 2006; WHO, 2004; Scholl and Johnson, 2000). Folic acid also plays an important role in the prevention of arteriosclerosis (Reynolds, 1996). Moreover, folates are required for the metabolism of homocysteine, whose level is associated with pregnancy complications, such as miscarriage, placental abruption, and hypertension disorders (Nelen *et al.,* 2000; Cotter *et al.,* 2001). Supplement of folic acid in peri-conceptional period could be a preventive factor for pregnancy depression(Xu *et al.,* 2014).In addition to the importance of folic acid supplementation on pregnant woman, many studies revealed its importance for her fetus. Adequate folate intake during the preconception period: before conception and throughout the first 12 weeks of pregnancy helps protect against a number of congenital malformations, including neural tube defects (NTDs) which are the second most common birth defects after congenital cardiac malformations (Cheschier, 2003). Neural tube defects are severe abnormalities of the central nervous system that developed in babies during the first few weeks of pregnancy resulting in malformations of the spine, skull, and brain; the most common neural tube defects are spina bifida (due to incomplete closure of the caudal neural tube), and anencephaly (due to incomplete closure of the rostral end of the neural tube).The double-blind, placebo-controlled, randomized trial rigorously conducted by the Medical Research Council in 1991 showed that supplementation with 4 mg of folic acid per day resulted in a 72% reduction in neural tube defect recurrence risk. Supplementation with folic acid has also been shown to reduce the risk consumed before and during pregnancy may reduce risk of: heart defects in infants (Bazzano, 2009), severe language delay in children at age 3 years (Roth *et al.,* 2011), autism spectrum disorder ASD (Rebecca and Daniel, 2012). In 2009 European Surveillance of Congenital Anomalies (EUROCAT) and US Preventive Services Task Force published that "many countries are recommended women planning to become pregnant receive 400 µg/day of folic acid at least one month prior to conception and for three months postconception".

WHO considers adherence to therapy is one of the important factors that affect the outcome of therapy. Many studies define adherence as the: "extent to which the patient's behavior matches agreed recommendations from the prescriber" (Kikkert, 2010; Sluijs *et al.,* 2006; Gray *et al.,* 2006; Hughes, 2004; Horne *et al.,* 2005).

Both self-report and the use of pill counts represent two methods of measuring adherence that are straightforward and can be utilized in clinical practice as part of the vital signs that patients receive at the beginning of their clinic visit. Barriers to adherence vary widely, and include concerns about efficacy, fear of side effects, inconvenience, poor doctor-patient relationship, lack of social support, patient motivation, or incorrect education regarding proper use (DiMatteo *et al.,* 1993, 2000).

For reasons related to the significance of folic acid supplementation for both a mother and her fetus, and a very little studies in the world and no previous studies in Thi-Qar city on adherence to folic acid alone that should be prescribed to the women at least two months before pregnancy and continued to the forth month of gestation. Consequently, an urgent need to assess the rate of adherence, the factors affecting the rate of adherence and the awareness among the pregnant women with folic acid supplements.

Subjects and method

A descriptive cross sectional study was conducted in medical care center in Suq-Al-Shuyukhcity in Thi-Qargovernorate from August 2014 to October 2014. A total of 136women were selected on the basis of inclusion criteria that is pregnant women of 20–45 years of age should be at the first trimester. Permission from head of the health care centers and was taken. From the pregnant women informed verbal consent also was followed. Detailed questionnaire was used to collect the data. Indirect methods of assessing medication adherence are more practical in everyday clinical practice. Of these, questionnaires, pill counts, prescription refill rates, patient self-reporting is the method that can be employed easily and relies on a trusting and engaging relationship between the patient and their provider if it is to be used accurately which are dependent in this study.

All women were interviewed and they were advised by their doctors to take one folic acid tablet 5 mg per day starting from one month at least before conception till 4th month of conception. The tablet used was supplied by Ministry Of Health for care centers. Each patient's adherence score was calculated as their days of drug acquired divided by their days in the study (days from first prescription fill to last prescription fill), using the methodology of Steiner and Prochazka (1997). High adherence was defined by an adherence score of greater or equal to 80% and non-adherent as an adherence score of less than 80%.Periodic visits were undertaken according to the prescription dates. During these visits folic acid tablet strip/blisters were cross checked for any remaining doses. The adherence to the folic acid tablets for that particular interval was calculated using the formula.

$$\text{Adherence rate (Bazzano, 2009)} = \frac{\text{No. of pills given} - \text{No. of remaining pills}}{\text{Expected number of pills to be taken}} \times 100$$

Statistical analysis

A Chi-Square test was conducted to assess the significance of associations among categorical groups, SPSS Software Version 17 was used, p-value of 0.05 or less was regarded as statistically significant.

Results and Discussion

The study includes one hundred and thirty six (136) pregnant women. The mean age of the participants is 26.7± 5.8 years. Table 1 shows that 42.65% of the study sample of younger than 25 years while women with 35 years or older reaches to 8.82%. On the other hand, women graduated from primary school comprise 36.76% which is the highest percentage of educational level of the study sample. Approximately thirty nine percent out of the 136 pregnant are of gravida 4 or more. Slightly more than the half consumes two, one or no medication per day. Based on the smoking status, the highest percentage of pregnant women belongs for non-smoker whereas the lowest one for ex-smoker, they comprise 54.42% and 45.58% respectively.

Table 2 represents the adherent status with folic acid in relation to pregnant medical history. Adherence to folic acid tablet appears satisfactory in 70(51.47%) and poor in 66(48.53%). In this study, the findings reveal only smoking status is insignificantly associates with drug adherence (p-value > 0.05) while age of the pregnant women and parity are statistically significant (p-value < 0.05). Furthermore, educational levels and number of medications used are of highly significant (p-value < 0.001) with folic acid adherence.

However, the knowledge of pregnant women about folic acid aspects are shown in the table 3 and reflects that most of pregnant women don't have enough information about folic acid, 44.12% of them don't know the folic acid regimen. The 20.58% thought that folic acid is administered to prevent anemia and unfortunately 64.70% don't know the benefit of folic acid during pregnancy. Further 42.64% don't know the time or when folic acid should be stopped and 23.52%suppose that it can be stopped when their health improvement is achieved. Again 64.70% believe it is more important in gravida1and 91.17% of pregnant women don't know the starting time of folic acid intake.

Women are especially susceptible to folate deficiency during pregnancy, which is a period of rapid fetal growth, organ differentiation and high rates of cell division (Tamura and Picciano, 2006; WHO, 2004; Scholl and Johnson, 2000). Usually a physician advices each woman to beware of ignoring folic acid administration particularly during the preconception period: before conception and throughout the first 12 weeks of pregnancy helps protect against a number of problems related to both the mother and her fetus.

As expected, not taking medication as prescribed—taking either too little, or too much, for too short, or too long a period, at the wrong time or in an ineffective way—can have negative consequences for patients, healthcare, and the economy. Thus, the primary goal of the current study was to identify current adherence to folic acid supplements within the field of pregnant women in Suq-Al-Shuyukh city.

High adherence was defined by an adherence score of greater or equal to 80% and non-adherent as an adherence score of less than 80%. This cut point is conventional in the adherence literature (Wei *et al.*, 2002) and yields measures of association that are easily interpreted.

Results of this study revealed that adherence to folic acid supplements was satisfactory in 51.47%that mean approximately half of this community was adhere to physician advise. This result is agreed with Mikkel Mylius study in 2010 where, only 51% of the pregnant women received FA supplementation in accordance with recommendations.

Unlike results of Rasmussen study in Denmark in 2010 (neither age nor smoking status of pregnant was significantly associated with adherence to folic acid supplementation), our results indicated that only smoking status of women was insignificantly related to their adherence. The analysis of this difference maybe the huge amount of responsibilities of the older age women in our country pay them to ignore her health.

Regarding the educational level, the current study showed that there was a significant association between nonadherence and low women education in agreement with outcomes of the study that done in Denmark (Knudsen *et al.*, 2004). It is a common belief that higher frequency of women adherence with higher educational level may be due to anxiety and high sureness in such groups.

It is well known that compliance is improved if the patient is taking single drug rather than two or more (WHO, 2007). Surprisingly, the present study showed that women taking three medications including folic acid supplement were more adherent to folic acid supplementation than those taking single medication which is reflected by the figures 51.42% and 40% respectively.

Table.1 Distribution of the pregnant' adherence according to their demographic characteristics

Variables	Frequency	Percentage %
Age		
< 25	58	42.65
25-29	28	20.59
30-34	38	27.94
≥35	12	8.82
Total	136	100%
Educational level		
Do not read and write	16	11.76
Read and write	8	5.88
Primary school graduate	50	36.76
Secondary school graduate	34	25
College and above	28	20.6
Total	136	100%
Parity		
gravida 1	24	17.65
gravida 2	44	32.35
gravida 3	14	10.29
gravida 4	54	39.71
Total	136	100%
No of medication administration		
≤ 2	74	54.41
3	50	36.77
4	10	7.35
≥5	2	1.47
Total	136	100%
Smoking status		
Smoker	0	0
Ex-smoker	62	45.58
Non-smoker	74	54.42
Total	136	100%

Table.2 Adherence rate in relation to Socio-demographic character

Character		Adherent (n=70)		Non-adherent (n=66)		Total	P-value
		No.	%	No.	%	No.	
Age (years)	- < 25	28	40	30	45.45	58	**0.028**
	- 25-29	12	17.14	16	24.24	28	**S**
	- 30-34	20	28.57	18	27.27	38	
	- ≥35	10	14.28	2	3.03	12	
Educational level	- Do not read and write	6	8.57	10	15.15	16	**0.000** **S**
	- Read and write	4	5.71	4	6.06	8	
	- Primary school graduate	30	42.85	20	30.30	50	
	- Secondary school graduate	16	22.85	18	27.27	34	
	- College and above	14	20	14	21.21	28	
Number of drugs	- < 3	28	40	46	69.69	74	**0.000**
	- 3	36	51.42	14	21.21	50	**S**
	- 4	6	8.57	4	6.06	10	
	- ≥5	0	0	2	3.03	2	
Smoking	- Smoker	-	-	-	-	-	**0.232**
	- Non-smoker	36	51.42	38	57.57	74	**NS**
	- Ex-smoker	34	48.57	28	42.42	62	
Parity	- Gravid 1	16	22.85	8	12.12	24	**0.009**
	- Gravid 2	18	25.71	26	39.39	44	**S**
	- Gravid 3	8	11.42	6	9.09	14	
	- Gravid 4	28	40	26	39.39	54	

Table.3 Knowledge of pregnant women about folic acid aspects

Folic acid aspects		Frequency	Percentage (%)
Do you know the regimen of folic acid?	- Yes	76	55.88
	- No	60	44.12
What is the benefit of folic acid during pregnancy?	- Don't know	88	64.70
	- anemia treatment	28	20.58
	- prevention of neural tube defects in fetus	20	14.70
Can folic acid be stopped when you want?	- Don't know	58	42.64
	- Yes	32	23.52
	- No	46	33.82
Dose it more important in gravid 1?	- Don't know	88	64.70
	- Yes	4	2.94
	- No	44	32.35
Do you know the starting time of folic acid supplement administration?	- Yes	12	8.82
	- No	124	91.17

Perhaps reflecting their awareness towered body health. However, multigravidae compared with primigravidae women were more likely to have followed the recommendations correctly (P= 0.009).

A common reason why patients don't take their medicines is simply forgetfulness (Cogswell *et al.,* 2003). In addition, there is low knowledge of our patients regarding folic acid supplements where only (55.88%) of participants know the regimen of folic acid supplement, 42.64%thought that they can stop administration of folic acid dependent on their desire, When they questioned about the benefit of folic acid supplementation during perconceptional period, only 14.7% of them answered correctly compared with 64.7% which have no information about its advantage.

Similarly, when questioned Dose it more important in gravid 1? Majority 64.7% answered "I do not know" results. However, 32.35% of individuals answered "No".

This may provide an explaining about poor communication between provider and pregnant or may reflect lack of knowledge about pregnant, inability to retain medical instructions, or other behavioural factors.

Medication adherence is a complex phenomenon with many causes. In this analysis, education level, patient satisfaction, and confidence were positively related to medication knowledge.

We also found unexpected relationship between the number of medicines and individuals' adherence, where better results were estimated for women that consumed multiple medicines per day than others.

In conclusion, this study revealed that the adherence rate is low. There are various causes that contribute to decreased adherence to folic acid supplementation including, educational level, age, misunderstanding of instructions, and multiple medications.

Recommendation

Improving adherence is a complex and variable process.

1. Provider training in adherence strategies is needed and should focus on communication skills, cultural sensitivity, and patient-centered interviewing as competencies that will improve patients' adherence.
2. Providers should seek opportunities to build patient confidence and enhance patient satisfaction through patient education and counseling.
3. Following the SIMPLE approach (Ashish Atreja *et al.,* 2005). This approach includes Simplifying the regimen, Imparting knowledge, Modifying patient beliefs, providing communication and building trust, leaving bias behind, and evaluating adherence.
4. Adherence requires the patient to believe there is a benefit to the medicine being prescribed and agree with instructions on how to take it.

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