Republic of Iraq Ministry of higher Education and Scientific Research Qadisiyah University Faculty of Pharmacy



Folic acid deficiency in pregnant women KAP Score in AL-Diwanyah

A project

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 السورة المجادلة الآية الأا

Dedication

To whom Allah sent as mercy to the worlds....

To the prophet Mohammed To all women in Iraq.... To my family..... To everyone I love.....

Acknowledgment

Praise be to god who enables our with his blessing to achieve this modest scientific effort.

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Abstract

Neural tube defects (NTDs), including anencephaly, encephalocele and Spina bifid are common causes of morbidity and mortality among infants an neonates. The NTDs incidence had been declined over last 50 years and is about 1-2 per 1000 babies folate deficiency is one of the important common vitamin deficiency in women. A low consumption of folate during pregnancy lead to poor outcome of pregnancy like NTDs. Seventy percent of NTDs are prevented by preconception of folic acid supplement.

A thirty pregnant women are interviewed in this study, only 30% had known about folic acid requirement in pregnancy, 16% of women are aware of the relation between folic acid and congenital abnormality in pregnancy 60% of sample had their knowledge from antenatal care units, there were 70% of the sample took folic acid in pregnancy but not in recommended doses. Only minority took it preconception.

Health care providers, including doctors, pharmacists, nurses and other society in the community should be play a professional role education women about the role of folic acid supplementation during pregnancy a preconception educational programs in TV or media and books magazines should be activated.

Aim of study was to study the knowledge, attitude and practice attitude of group of pregnant women about the role of folic acid in pregnancy, women are interviewed from AL-Diwanyah maternity and pediatric hospital and AL-Hamza hospital and from private clinics by a questionnaires about knowledge, A attitude and practice about folic acid in pregnancy and demographic data were obtained from them

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Chapter One

Introduction:

Folic acid is a vitamin B_9 , it's a synthetic form of folate. It is completely oxidized monoglutamy form of the water -soluble vitamin commercially present in certain foods, including dark green leafy vegetables⁽¹⁾. Vitamin B₉ include both folate and folic acid and it's many body functions. It's good ingredient in producing nucleic acid that forms part of genetic materials⁽²⁾. Folic acid important for creating RBCs, preserving the brain health of infants, reduced cell growth and destruction of cell division are possible effects of an absence of folic acid, and it is important in providing cell division and growth such as in infancy and pregnancy⁽³⁾. The top priority for any society is healthy start in life⁽⁴⁾. Neural tube defects (NTDs) are among the most frequent congenital malformations⁽⁵⁾. congenital anomalies define as decreasing in cell growth and destruction of cell division that are possible effects of folic acid deficiency $^{(2)}$. To avoid congenital anomalies there are many interventions: avoidance of certain environmental exposures, adequate nutrition folate and other vitamin intake, cessation of alcohol and smoking consumption, prevention and control of maternal infection disease⁽⁷⁾. Globally, an estimated two billion people are affected by deficiencies of essential vitamins and minerals, collectively known as hidden hunger, many countries in sub-Saharan Africa as well as in India and Afghanistan, had high level of hidden hunger with shunting, iron deficiency anemia and vitamin deficiency⁽⁸⁾. Malnutrition during associated with many disease effect on newborns. According to research, there is significant dose response relationship between folate intake and birth weight. This relationship indicate 2% increase in birth weight for every two fold increase in folate intake⁽⁹⁾. Maternal folate deficiency associated with neural tube defects (NTDs)⁽¹⁰⁾. Folic acid deficiency in pregnancy also associated with autism in newborn infants⁽⁹⁾.

Chapter Two

2.1. Folate and folic acid

Folate is one of the water-soluble B vitamins; Folic Acid (FA) is the synthetic form of this vitamin and is only minimally different from folate. FA has the advantage of being better absorbed by the body and having a much higher bioavailability than naturally occurring folate.⁽¹¹⁾ Being water soluble, folate is easily excreted by the body and is not stored, such that an adequate daily intake is necessary to maintain the required blood levels of this vitamin. The National Institute of Health – Office of Dietary. Supplements in the UK⁽¹²⁾ gives the daily recommended dietary allowance (RDA) of folate for an adult male or female 400 micrograms, this requirement increases to 600 as micrograms of dietary folate in pregnancy.

2.2. Nature of the folic acid

(What to know about folic acid)⁽¹³⁾

Folic acid is a form of vitamin B_9 that can dissolve in water. It is a very ingredient in the making of the nucleic acid that forms part of all genetic material.

It is a complex B vitamin, similar to vitamin B_{12} , vitamin B_9 and its forms carry out the crucial functions of creating move red blood cells. Preventing hearing loss and preserving the brain health of infants.

According to the British Dietetic Association (BDA) folic acid is vital for making red blood cells as well as

*The synthesis and repair of DNA and RNA.

*Aiding rapid cell division and growth.

*Enhancing brain health.

*Age related hearing loss.

It is particularly important for women who are pregnant to consume enough folic acid, to prevent the fetus from developing major congenital deformities of the brain or spine including neural tube defects, such as spina bified and anccephaly. Women planning to get pregnant should take folic acid supplements for full year before conception to reduce the risk of these developments⁽¹¹⁾.

2.3. The natural source of folic acid

Is dark green vegetables are good source of folic acid⁽¹⁾. Be careful not to overcook them as the folic acid content can drop considerably when exposed to heat. The following food are known to be rich in folic acid:

Asparagus Baker's yeast Broccoli Cabbage Cauliflower Egg yolk Jaket potato Kidney Lentils Lettuce Liver, although women shouldn't consume this during pregnancy Many fruits, especially papaya and kiwi Milk Oranges Peas Spinach Sunflower

Seeds

Whole wheat bread as it is usually fortified

2.4. Pathophysiology

Folic acid is composed of a pterin ring connected to paminobenzoic acid (PABA) and conjugated with one or more glutamate residues. It is distributed widely in green leafy vegetables, citrus fruits, and animal products. Humans do not generate folate endogenously because they cannot synthesize PABA, nor can they conjugate the first glutamate. Folates are present in natural foods and tissues as polyglutamates because these forms serve to keep the folates within cells. In plasma and urine, they are found as monoglutamates because this is the only form that can be transported across membranes. Enzymes in the lumen of the small intestine convert the polyglutamate form to the monoglutamate form of the folate, which is absorbed in the proximal jejunum via both active and passive transport. Within the plasma, folate is present, mostly in the 5-methyltetrahydrofolate (5-methyl THFA) form, and is loosely associated with plasma albumin in circulation. The 5methyl THFA enters the cell via a diverse range of folate transporters with differing affinities and mechanisms (ie, adenosine triphosphate [ATP]-dependent H+ cotransporter or anion exchanger). Once inside, 5methyl THFA may be demethylated to THFA, the active form participating in folate-dependent enzymatic reactions. Cobalamin (B-12) is required in this conversion, and in its absence, folate is "trapped" as 5methyl THFA. From then on, folate no longer is able to participate in its metabolic pathways, and megaloblastic anemia results. Large doses of supplemental folate can bypass the folate trap, and megaloblastic anemia will not occur. However, the neurologic/psychiatric abnormalities associated with B-12 deficiency ensue progressively. The biologically

active form of folic acid is tetrahydrofolic acid (THFA), which is derived by the 2-step reduction of folate involving dihydrofolate reductase. THFA plays a key role in the transfer of 1-carbon units (such as methyl, methylene, and formyl groups) to the essential substrates involved in the synthesis of DNA, RNA, and proteins. More specifically, THFA is involved with the enzymatic reactions necessary to synthesis of purine, thymidine, and amino acid. Manifestations of folate deficiency thereafter, not surprisingly, would involve impairment of cell division, accumulation of possibly toxic metabolites such as homocysteine, and impairment of methylation reactions involved in the regulation of gene expression, thus increasing neoplastic risks. A healthy individual has about 500-20,000 mcg of folate in body stores. Adults need to absorb approximately 400 mcg of folate per day in order to replenish the daily degradation and loss through urine and bile. Otherwise, signs and symptoms of deficiency can manifest after 4 months. The degree of folate absorption depends on its source. Approximately 50% of folate naturally occurring in food is bioavailable, whereas nearly 100% of folic acid supplements are absorbed when consumed fasting, and approximately 85% of folic acid supplementation is absorbed when consumed with $food^{(14)}$.



Structure of folic acid

2.5 Deficiency

A folate deficiency can occur when the need for folate by the body is increased, as in pregnancy or lactation, when dietary intake of folate is inadequate, and when the body excretes more folate than usual. Malabsorption syndromes, alcoholism and drug abuse can cause deficiency as can certain drug treatments or use of over-the-counter pain relievers like non- steroidal anti-inflammatory medications (NSAIDS) or aspirin.

Signs of folic acid deficiency are subtle and include diarrhea, loss of appetite, pale skin, nausea, and weight loss with poor absorption of other nutrients.

Women with inadequate folic acid intake are more likely to give birth to low birth weight babies (less than 5 $\frac{1}{2}$ pounds) and premature infants as well as to infants with neural tube defects (NTDs). These defects may involve the brain, spinal cord, membranes and skull⁽¹⁵⁾.



2.5.1 Folic acid and neural tube defect

NTDs are major birth defect resulting from inappropriate development of neurological system in early embryonic growth⁽¹⁶⁾. The major NTDs encountered are anencephaly and spina bifida, which occur when the neural Tube fails to close. These defect are associated with sever morbidity and mortality, causing distress to both the individual and his family and presenting a significant burden to public health⁽¹⁷⁾. Spina bifida: incomplete development of the spinal cord or vertebrae A anencephaly: incomplete development of the major part of brain.



Figure 1: Embryonic development and spina bifida (By permission of Mayo Foundation for Medical Education and Research.

2.5.2. Prenatal screening and diagnosis of neural tube defects

When apparent or previous sibling has had an NTD, the risk of recurrence is 5-10% mid trimester maternal serum alpha-fetoprotein (APP) levels are increased in pregnancies affected by open (NTDs). These are once used as the established screening tests for NTDs with screening positive women being referred for amniocentesis. The presence of acetyl cholinesterase (a central nervous system neuro transmitter) in amniotic fluid was taken as being diagnostic of an open NTD. The need for twostep screening/ diagnosis process was quickly superseded by the development of high resolution ultrasound.

Anencephaly and encephaloceles are detectable on first trimester ultrasound if an adequate examination of the cranial vault is performed Spina bifida, on the other hand, requires the systematic detailed examination of fetal spine. At the routine 20 week anomaly scan. The diagnosis may be suspected from the visualization of the "lemon" shape of skull and "banana" (absent of cerebellum) sign in the fetal brain at this examination. The sensitivity of ultra sound for both open and closed defects and NTDs is greater than 95%. Other central nervous system abnormalities (not strictly NTDs), such as hydro cephalous, can also be detected at the 20 week scan⁽¹⁸⁾.

2.5.3. Prevention of neural tube effect NTD

A. folic acid supplement taken before and during pregnancy can reduce the occurrence of neural tube defect⁽¹⁹⁾

B. for women of child bearing potential at high risk of having a pregnancy affected by NTD (e.g. if they have had a previous pregnancy affected by a neural tube defect), the dose of folic acid is 4 or 5 mg daily starting before pregnancy (in USA the recommendation is 4 week before) and continued through the first trimester (until week 12 of pregnancy)⁽¹⁹⁾

C. for women at a low risk of having a child with a NTD the dose is 400 mcg daily and continued through the first trimester (until week 12 of pregnancy)⁽¹⁹⁾

2.5.4. Folic Acid Supplementation and Birth defect other than neural tube defect.

Folic acid supplementation has been shown to benefit other congenital anomalies, such as congenital heart defect⁽²⁰⁾, urinary tract anomalies⁽²¹⁾, oral facial clefts⁽²⁰⁾, limb defect⁽²⁰⁾, pyloric stenosis⁽²²⁾. A recent review⁽²³⁾ summarizes the recent literature regarding prevention of congenital anomalies with pre conceptional folic acid supplementation.

2.5.5. Other indications for folic acid⁽²⁰⁾

- A. folate deficient megaloblastic anaemia
- B. Prevention of methotrexate induce side effect
- C. Prophylaxis of folate deficiency in dialysis

2.5.6. Folic Acid needs

The current recommendation for folic acid is 400 mcg per day for adult women. Pregnant and lactating women require more, at level of 600 mcg 1 day and 500 mcg 1 day, respectively (table 1). Recent study evaluating folate intake among college –educated women showed that 36 percent of those who were pregnant and 32 percent of those lactating were not able to meet daily folate requirements C600 mcg and 500 mcg, respectively⁽¹⁵⁾.

Age group	Male & females	Pregnancy	Lactation	
	(mcg folate, day)	(mcg folate, day)	(mcg folate, ay)	
9-13	300	-	-	
14-18	400	600	500	
194	400	600	500	

Table 1 folate needs for adult

Institute of medicine, national academy of science, 2002

6- Role of pharmacists

The pharmacist has a critical role in the treatment of patients with folic acid deficiency in pregnancy . Pharmacists can assist patients with therapy management, particularly in areas of folic acid administration, dietary recommendations, drug interactions with oral iron, and medications that can exacerbate conditions. As pharmacists, we should also be aware of the signs and symptoms of folic acid deficiency in order to assess efficacy of treatment and refer those patients who need to seek medical attention. Pharmacists can utilize their extensive pharmacological knowledge to increase positive outcomes in our patients⁽²⁵⁾.

Chapter Three

3.1. Patients and Methods

The aims of study to asses three questions, first to assess the folic acid level of awareness in AL-Diwaniya pregnant women including their knowledge of it's natural sources, using in preventing of Neural tube defects and preconceptional intake.

Second to assess the actual in taking of folic acid during pregnancy and preconceptional period and third to explore the attitude regarding folic acid taking.

3.2. Setting

Across – Sectional study was conducted in AL-Diwaniya Maternity and Teaching hospital and AL-Hamza hospital and clinic private from the 1st of December to the end of March 2018. The number of pregnant women were 30 were included all pregnant women an age from (17 -40) years, all married women and an Ethical approval was obtained from responsible authorities of hospitals a clinic private participant consent was obtained.

3.3. Data collection

Data were collected by direct interview using a questionnaire. The questionnaire are included four domains demographic data, knowledge, attitude and practice of pregnant women regarding folic acid supplementation.

Folic acid deficiency KAP scour

Patient name:Age:Gestational age:Type of infertility:Primigravida:Multigravida:Husband name:Age:Monthly income:Academic achievement:Yes/No

Questions	Yes/No
1- Do you have abortion?	
2- Do you have congenital anomaly?	
3- Do you have neural tube defects?	

Knowledge (if strongly agree = 5, 75% agree = 4, undetermined = 2,

strongly disagree =1)

Questions	Answer of patients	Degree
1- In pregnancy, is there is need for folic acid		
Supplement?		
2- Do you know there is relationship between		
folic acid deficiency and congenital abnormality		
in pregnancy?		
3- Do you are going to Antenatal care?		
4- In the first trimester of pregnancy, is the folic		
acid intake important?		
5- Are you watching T.V and programs		
About folic acid deficiency in pregnancy?		
6- Does your doctor advise you about folic acid?		
7- Do you know about folic acid rich food		
sources?		

Attitude(if strongly agree = 5, 75% agree = 4, undetermined = 3, not agree = 2

Questions	Answer of patients	Degree
1- Will folic acid deficiency lead to abnormality		
in newborn?		
2- Are you know more about folic acid?		
3- What your opinion about program of		
antenatal care?		
4- Do you think in your age there is congenital		
abnormality?		
5- What your opinion about folic acid?		

strongly disagree =1)

Practice (If Yes = 1, No = 0)

Questions	Yes/No	Degree
1- Did you take folic acid supplement in		
Pregnancy?		
2- Do you have intake folic acid rich food?		
3- Do you forget taking folic acid dose		
sometimes?		
4- Do you are ignoring taking the dose of folic		
acid?		
5- Do you are taking folic acid in preconception		
period?		

3.4. Analysis

Statistical analysis was carried out using spss version 12, confidence intervals (I) are given at 95% level of confidence simple logistics regression analysis was done using age, parity, education and knowledge of the mothers about folic acid on pregnancy.

Chapter Four

4.1. Result

Table 1

The number of mothers are 30 were included in the study mean age 24 – 6 ∓ 6.2 , range (17 – 37) years the husband ages mean 30.7 \mp 5.8, range (20 – 41) years. The a gestational age range (4 – 36) wk. There are 20% of primigravida and 80% of multigravida, and those have good economic status 10%, poor economic 90%.

According Academic qualification primary school 46% secondary school 3%, higher education 50%. Those cases had 33% of abortion, 6.7% history of congenital abnormalities and 6.7% Neural tube defects.

Table 2

Which demonstrate the knowledge about folic acid among studied sample.

There is twenty – seven percent of the sample knew about the need of folic acid in pregnancy, sixteen percent of the sample knew about the risk of deficiency of folic acid in pregnancy. One third of the sample don't know the proper time of taking folic acid.

One quarter of the sample their knowledge were taking from the antenatal care units.

Two third from studied women don't know the food items rich in folic acid.

Table 3

Shows the studied pregnant women and their attitude and their openion about folic acid deficiency risk and relation to congenital anomaly responded variably to this question 23% undetermined answers. Also their opinion about who were needed more information about folic acid supplements during pregnancy, 23% variable answers between positive and negative. About programs of antenatal care, one third of studied pregnant women gave positive opinion.

Table 4

Shows the answers of questions about practice of taking folic acid. Seventy percent of sample are taking folic acid incurrent pregnancy.

Thirty – six percent of studied sample are taking food rich in folic acid, 70% of studied women forget taking folic acid supplement. Ninety percent of pregnant women don't taking folic acid before pregnancy.

Table 5

Shows the total knowledge score mean 18.30, total attitude score mean 12.13 and total practice score mean 2.57.

Table 6

The correlation between women age, gestational age, income, education, Abortion, congenital anomaly and NTD. Each parameter if compared with total knowledge total attitude and practice no significant correlation P value > 0.01. Only there is a relation between congenital anomaly and total attitude P value < 0.012.

4.2. Statistical analysis

Results

 Table 1: Demographic characteristics of the study population

Characteristic	Value
Number of cases	30
Women age	
Mean ±SD years	24.67 ±6.21
Range (minimum – maximum) years	20 (17-37)
Husband age	
Mean ±SD years	30.70 ±5.87
Range (minimum – maximum) years	21 (20-41)
Gestational age	
Mean ±SD weeks	22.97 ±10.90
Range (minimum – maximum) weeks	32 (4-36)
Primipara; n (%)	6 (20)
Multigravida; n (%)	24 (80)
Economic status	
Good	3 (10)
Poor	27 (90)
Academic qualification	
Primary	16 (46.6)
Secondary	1 (3.3)
Higher education	15 (50)
Abortion	10 (33.3)
Congenital abnormalities	2 (6.7)
Neural tube defects	2 (6.7)

Table 2: Knowledge

Scor e	k1	k2	k3	k4	k5	k6	k7
1	15 (50.0)	16 (53.3)	3 (10.0)	10 (33.3)	21 (70.0)	5 (16.7)	18 (60.0)
2	0 (0.0)	1 (3.3)	2 (6.7)	4 (13.3)	5 (16.7)	0 (0.0)	1 (3.3)
3	6 (20.0)	8 (26.7)	4 (13.3)	7 (23.3)	1 (3.3)	6 (20.0)	9 (30.0)
4	1 (3.3)	0 (0.0)	14 (46.7)	2 (6.7)	2 (6.7)	9 (30.0)	0 (0.0)
5	8 (26.7)	5 (16.7)	7 (23.3)	7 (23.3)	1 (3.3)	10 (33.3)	2 (6.7)
Total	30	30	30	30	30	30	30
Total	(100.0)	(100.0)	(100.0)	(100.0)	(100.0)	(100.0)	(100.0)

Table 3: Attitude

Score	A1	A2	A3	A4	A5
1	17 (56.7)	17 (56.7)	2 (6.7)	9 (30.0)	11 (36.7)
2	3 (10.0)	2 (6.7)	4 (13.3)	7 (23.3)	2 (6.7)
3	7 (23.3)	7 (23.3)	12 (40.0)	10 (33.3)	13 (43.3)
4	0 (0.0)	2 (6.7)	5 (16.7)	2 (6.7)	1 (3.3)
5	3 (10.0)	2 (6.7)	7 (23.3)	2 (6.7)	3 (10.0)
Total	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)

Table 4: Practice

Score	P1	P2	P3	P4	P5
0	9 (30.0)	19 (63.3)	9 (30.0)	9 (30.0)	27 (90.0)
1	21 (70.0)	11 (36.7)	21 (70.0)	21 (70.0)	3 (10.0)
Total	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)	30 (100.0)

Table 5: Total score

Score	Minimum	Maximum	Mean	SD
Total k	9.00	34.00	18.30	6.66
Total A	5.00	23.00	12.13	4.44
Total P	1.00	4.00	2.57	0.77

Table 6: Correlations

Chamaataristia	Paramete	Total	Total	Total
Characteristic	r	knowledge	Attitude	Practice
Age	r	0.305	0.282	-0.340
	Р	0.102	0.131	0.066
Age Husband	r	0.252	0.137	-0.341
	Р	0.179	0.472	0.065
GA	r	-0.296	-0.001	-0.014
	Р	0.112	0.994	0.941
Gravida	r	0.036	0.111	-0.175
	Р	0.852	0.56	0.354
Income	r	-0.032	-0.188	0.190
	Р	0.866	0.319	0.315
Education	r	0.012	-0.025	0.101
	Р	0.951	0.895	0.596
Abortion	r	-0.259	0.059	0.031
	Р	0.167	0.755	0.871
Congenital aomalies	r	0.273	0.451	-0.199
	Р	0.144	0.012	0.292
NTD	r	0.090	0.176	-0.023
	Р	0.637	0.353	0.902

4.3. Discussion

This study aimed to identify current levels of knowledge ,attitude and practice regarding use of folic acid among pregnant women and to determine factors influencing these. It was found that the overall knowledge regarding folic acid in this study population was 18.3. Different finding had been observed in different studies worldwide in developing as well as developed countries. The level of knowledge was poor among the pregnant mothers and postpartum women of United Arab Emirates⁽²⁶⁾.

The study also revealed that mothers who were less educated had a poorer knowledge than others. Lower education may be a barrier in being able to come across key messages regarding folic acid either because of the forums where it is discussed or the content, both of which may not reach sections of society with lower levels of education. In North China where the prevalence of NTDs is high, knowledge was found low among the less educated women⁽²⁷⁾.

Lower socio economic status also was associated with poorer knowledge both in this study as well as in other countries and is perhaps linked to lower levels of education among such groups. Like other studies this study also did not find any association between level of knowledge and age, obstetric score, duration of gestational period, number of ante natal visits⁽²⁸⁾. While one assumes that subjects who had a previous bad pregnancy outcome would have better knowledge about folic acid, this study did not reveal any such association.

Health education among the women of child bearing age can improve the knowledge. Studies have suggested on greater emphasis for strategies to improve the levels of folic acid knowledge and folic acid supplementation for those with poor knowledge⁽²⁹⁾. Pre and post health education level of awareness regarding folic acid in Netherland showed marked improvement of knowledge after health education⁽³⁰⁾.

This present study revealed a low negative attitude of the interviewed women about their opinion about the folic acid usefulness in pregnancy and 40% women had positive attitude about the role of antenatal care units in providing knowledge about folic acid. Other study had revealed a positive attitude 88% toward retaking of folic acid supplement in future pregnancy⁽³¹⁾.

In this study the practice was good and it's mean value about 2.57 .The good practice not due to education of patient only but the health care providers doctors and pharmacists played an important role in increasing women's awareness about the role of folate in pregnancy as mentioned by 2.5 of the pregnant women participating in this study, while the role of nutritionists was not encouraging. Previous experience was the second commonest source of knowledge. Agnieszka et al. reported that magazines and newspapers were the most commonly cited source of knowledge in their study followed by leaflets and general practitioners⁽³²⁾. Although a programme to increase dietary folate intake of potential mothers may be effective in reducing NTDs, the only proven and practical preventive measure currently available is to take oral multivitamin supplements containing folic acid. Multivitamin supplementation has also been associated with the reduced incidence of other congenital malformations⁽³³⁾. Concerning the behavior of women regarding folate supplementation

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Chapter Five

5.1. Conclusion

Health care providers, including doctors, pharmacists, nurses and other society in the community should be play a professional role education women about the role of folic acid supplementation during pregnancy a preconception educational programs in TV or media and books magazines should be activated.

5.2. Recommendation

1- Women in reproductive age group should be advised about the benefits of folic acid supplementation during wellness visits (birth control renewal, pop testing, yearly examination), especially if pregnancy is contemplated.

2- Women should be advised to maintain a healthy nutritional diet, good or excellent sources of folic acid: broccoli, spinach, peas, corn, beans, oranges.

3- Women who could become pregnant should be advised to take a multivitamin containing 0.4 mg to 1.0 mg of folic acid daily.

4- Women taking a multivitamin with folic acid supplement should be advised not to take more than 1 daily dose of vitamin supplements as indicated on the product label.

5- Women in intermediate to high risk categories for NTDs (NTD affected previous pregnancy, family history, insulin dependent diabetes, epilepsy treatment with valproic acid or carbamazepine)

Should be advised that high dose of folic acid (4 mg - 5 mg daily) supplementation is recommended. This should be taken as folic acid alone, not in a multivitamin forms, due to risk of excessive intake of other vitamin such as vitamin A.

6- The choice of a 5 mg folic acid daily dose for women considering a pregnancy should be made under medical supervision after minimizing B_{12} deficiency.

7- Sign and symptom of vitamin B_{12} deficiency should be considered before initiating folic acid supplementation of dose greater than 1 mg.

8- Women who become pregnant should be advised of availability of noninvasive screening tests and invasive diagnostic tests for congenital birth defect (including NTD): maternal serum "triple marker screen" at 15 – 20 weeks, ultra sound at 16 to 20 weeks, and amino – centesis after 15 weeks of pregnancy if a positive screening test is present.

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