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Role of Folate and Folic Acid During Pregnancy

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Abstract: ***Pregnancy represents a period of fast tissue growth of maternal and foetal tissues that's related to enhanced energy and nutrient needs. Maternal nutrition throughout gestation period, has being essential for best offspring development, reducing long unwellness burden and for general health throughout life. Maternal Folate throughout pregnancy might have numerous roles in offspring health, as well as neurodevelopment and psychological feature performance in childhood.***
Folate is crucial for C1 metabolism, a network of pathways concerned in many biological processes as well as nucleotide synthesis, deoxyribonucleic acid repair and methylation reactions. The periconceptional use of pteroylglutamic acid (Folic Acid) containing supplements reduces the primary incidence, as well as recurrence of neural tube defects. Folic Acid (FA) are artificial form of a necessary vitamin generically considered Folates or B9. It is concerned in one-carbon metabolism, and it's been connected to lowering neural tube Defect (NTD).
National programs to mandate fortification of food with Folic Acid have reduced the prevalence of NTDs worldwide . The indisputable protecting role of Folic Acid in the hindrance of NTD, in addition to the low compliance of women to Folic Acid recommendations, has aroused the choice of mandatory Folic Acid fortification, a policy currently in place in over eighty countries worldwide. Mandatory food fortification needs food makers to feature Folic Acid to certain foods (e.g. starch or grain products), whereas voluntary fortification permits Folic Acid to be added to foods at the discretion of manufacturers. Food fortification with Folic Acid because the intervention is likely to achieve increasing Folic Acid intake among populations throughout the world. The objective of this article is to discuss the Role of Folic Acid and Folate during pregnancy and to review the role of Folate and Folic Acid , metabolism , absorption and Folic Acid effects on maternal on the basis of recent findings that are important for implementation of fortified food to design future studies.
Keywords: Neurodevelopment, Methylation Reactions, Pteroylglutamic Acid, Bioavailability, Monoglutamates.

I. INTRODUCTION

Pregnancy is recognized as a time when Folic Acid necessities are increased to sustain the demand for speedy biological process and growth of foetal, placental and maternal tissue. Folic Acid (FA) is the artificial form of a vital vitamin generically considered as Folates or B9. it's concerned in one-carbon metabolism, and it's been connected to lowering neural tube Defect (NTD) risk once taken as a supplement round the time of conception Folates also are naturally present in foods like green leafy vegetables, fruits, liver, legumes, and nuts. Folic Acid encompasses a major role in the synthesis of deoxyribonucleic acid and other crucial cell components and is therefore an important nutrient throughout the lifetime and particularly in phases of rapid cell growth.There are several crucial cellular pathways dependent on Folate as a one-carbon source, as well as deoxyribonucleic acid, RNA, and protein methylation, as well as DNA synthesis and maintenance.

Neural tube defects (NTDs) occur when the neural tube fails to close early in embryonic development, leading to damage to the exposed underlying neural tissue. These birth defects may result in vital morbidity and mortality depending on the placement and severity of the lesion.The neural tube closes early in embryonic development (28 days after conception), thus a woman ought to begin pteroylmonoglutamic acid supplementation ideally before becoming pregnant.There is convincing proof that the chance of NTD may be reduced by improving the Folate status of women some weeks before conception and/or throughout the first weeks of gestation period. Few approaches will increase intake of Folate/Folic Acid: dietary improvement, supplementation, and food fortification. Supplementation alone also has not been an efficient approach because approximately 50% of pregnancies are unplanned. Fortifying foods with pteroylmonoglutamic acid has been a extremely effective and additional uniform intervention, as a result of fortification makes pteroylmonoglutamic acid accessible to all women of childbearing age while not requiring behavior modification. Fortification of flour with Folic Acid encompasses a evidenced record of hindrance of NTDs in developed countries. By continuing to extend the amount of states with programs to fortify flour with pteroylmonoglutamic acid, we have the chance to deliver a proven prevention effort for families and to assist tens of thousands of babies round the world to be born healthy rather than paralyzed or dying from NTDs.[1]

II. RECOMMENDATIONS FOR PRECONCEPTION AND PREGNANCY

A. *Folic Acid and Folate*

Folic Acid (FA) is the synthetic form of an essential water-soluble vitamin generically regarded as Folates or B9. It is involved in one-carbon metabolism, and it has been linked to lowering Neural Tube Defect (NTD) [2]. Folates are also naturally present in foods such as green vegetables, fruits, liver, legumes, and nuts [2].The major food sources of Folate include cooked dried beans,leafy green vegetables, and fortified cereals[3].

B. *Dietary Folate Intake*

According to the world Health Organization guideline, daily Folic Acid supplementation is usually recommended as a part of the antenatal care to reduce the risk of low birth weight, maternal anemia, and iron deficiency. Folic Acid is usually recommended at the daily supplemental dose of 400 (0.4 mg) throughout gestation period.. Folic Acid supplementation is usually recommended to start as early as possible in all pregnant adolescents and adult ladies. [4]

Indian Council of Medical research recommends 200 μg because the intake of dietary Folate for adult females taking the present level of intake and therefore the prevalence of sub-clinical deficiency into thought. a further demand of 300 μg , respectively, throughout pregnancy and lactation was determined to be added for meeting the factorial additional needs. available evidence indicates that 0.4 mg (400 μg)/day of Folic Acid will reduce the amount of cases of NTDs. subsequently, the Institute of medication (IOM) in 1998 declared that women capable of becoming pregnant ought to consume 400 of Folic Acid daily from fortified foods or supplements, or both, additionally to that obtained through a normal diet. [4]

During pregnancy, Folate needs rise because of the increased cellular division and metabolism associated with placental and foetal development, uterine enlargement, and maternal blood volume expansion. the higher dietary Folate recommendations for pregnant women are difficult to satisfy by increased consumption of Folate-rich food products. more effective methods to extend the Folate intake include vitamin supplements and consumption of fortified food products .The use of Folic Acid containing dietary supplements is the simplest measure for increasing Folate status [5]

SUMMARY OF RDA FOR INDIANS -2020

AGE GROUP	CATEGORY OF WORK	BODY WEIGHT	FOLATE (μg/d)
MEN	Sedentary	65	250
	Moderate		
	Heavy		
WOMAN	Sedentary	55	180
	Moderate		
	Heavy		
	Pregnant women	55+10	480
	Lactation (0-6m)		280
	7-12m		280
INFANTS	0-6 m*	5.8	-
	6-12m*	8.5	71
CHILDREN	1-3Y	12.9	90
	4-6Y	18.3	111
	7-9Y	25.3	142
Boys	10-12 y	34.9	180
Girls	10-12 y	36.4	186
Boys	13-15 y	50.5	238
Girls	13-15 y	49.6	204
Boys	16-18 y	64.4	286
Girls	16-18 Y	55.7	223

*Adequate Intake (AI)
(ICMR , NIN - 2020)

C. *Peri-conceptional Folic Acid Supplementation*

Women of childbearing age, i.e. people who are 'at risk' of becoming pregnant, and pregnant women within the first trimester are recommended to take at least 400 ug folic acid per day from supplements, fortified foods, or both to cut back their risk of having an NTD-affected pregnancy. women are suggested to start taking folic acid supplements a minimum of one month before becoming pregnant. Preferably, the dose of folic acid ought to be chosen depending on the potential time before pregnancy: pteroylmonoglutamic acid status will increase faster with 800 ug/day folic acid compared to 400 ug/day folic acid. [5]

Women should be made aware to get optimum intakes of pteroylmonoglutamic acid, because the closure of neural tube happens by day 28 post-conception, the timing of usage of pteroylmonoglutamic acid supplement is extremely vital to stop pregnancies affected by NTDs. [5]

D. Role of Folate in Pregnancy

Folate requirements rise during pregnancy to keep up with the demand for rapid cell division and expansion in foetal, placental, and maternal tissue. Folate is essential for DNA, RNA, and protein production, as evidenced by this. In addition to the physiological changes associated with the growth of maternal and foetal tissues, there is a 50% increase in plasma volume when compared with an increase in the erythrocyte mass by 25 %, increasing the demand for Folate. [6]

III. OPTIMISING FOLATE STATUS IN WOMEN OF REPRODUCTIVE AGE

A. Food Folates, Folic Acid and Bioavailability

Individuals and populations can obtain appropriate Folate levels through three methods: naturally occurring food Folates, fortified foods, and supplements. Food folates are mostly polyglutamy and must be converted to monoglutamates in order to be absorbed, whereas FA, the synthetic vitamin form found in fortified foods and supplements, is a monoglutamate.

Natural Folates are reduced molecules, whereas FA is completely oxidised. As a result, as compared to FA at equivalent ingestion levels, naturally occurring dietary Folates show insufficient bioavailability. Aside from their low bioavailability once inside the body, food Folates are intrinsically unstable during cooking, which can significantly lower the Folate content of this product before it reaches the consumer.

FA, on the other hand, is a very stable and bioavailable form of the vitamin. When taken as a supplement, FA is thought to have a 100% bioavailability, but FA in fortified foods is predicted to have roughly 85% of the bioavailability of FA supplements. Because natural food Folates are unstable and bioavailable, the possibility to improve Folate status only through food Folates is limited.[6]

FOOD	SERVING SIZE	FOLIC ACID AMOUNT* (MICROGRAMS)	FOLATE AMOUNT (MICROGRAMS DFE**)
GRAIN FOODS			
Macaroni , Cooked	1 cup	80-90	140-160
Noodles , cooked	1 Cup	90	160
White rice cooked	1 Cup	95	170

* Synthetic folic acid content. ** DFE = dietary folate equivalents. Micrograms DFEs = food folate content + (folic acid content x 1.7). The DFE takes into account that synthetic folic acid is better absorbed than foods with the natural form of the vitamin

FOOD	SERVING SIZE	FOLATE AMOUNT (MICROGRAMS DFE**)
FRUITS		
Banana	1 Medium	20
Grapes	1 Cup	40
Orange	1 Medium	40
VEGETABLES		
Okra, cooked (ladies fingers)	1/2 cup	135
Spinach, raw	1 cup	110
Tomato juice	1 cup	50
DAIRY		
Milk	1 Cup	10-15
Cheese , American or hard cheese (cheddar etc)	1 ¼ Inch cube	5
MEAT , POULTRY , FISH , DRY BEANS , EGGS & NUTS		
Beans , cooked	½ Cup	115-145
Egg	1, large	25
Meat , fish , poultry (not breeders or batter fried)	30 ounces, size of a deck of cards	5-15
Peanut butter	2 tablespoon	25

* DFE = dietary folate equivalents. Fruits, vegetables, dairy foods, meat, poultry, fish, dry beans, eggs and nuts do not contain synthetic folic acid.

Source: Bailey and Suitor, Journal of the American Dietetic Association, 2000 except USDA National Nutrient Database for Standard Reference, Release 17. Accessed February 8, 2005.All foods are enriched or made with enriched flour unless otherwise noted. Not enriched. (florida Folic Acid coalition , last modified ; 06/08/2017)

B. Intestinal Absorption of Folic Acid

Folates are polyglutamates in the food and must be transformed enzymatically into Folate monoglutamates by Folate reductase in the jejunal mucosa in order to be absorbed. Folic Acid, on the other hand, is absorbed two times better than Folates. Because natural dietary folates are highly unstable molecules, vitamin activity is likely to be lost during food processing.

C. The effect of Different Cooking Methods on Folate Retention

The amount of folate retained in various foods varies greatly depending on the food and the cooking method. Animal-derived folates (such as beef) have been discovered to be resistant to cooking for long periods of time. Similarly, when potatoes were cooked, folate was well retained. However, it was discovered that the method and length of time used to cook green vegetables had a significant impact on folate retention from this important food source of folate. [7]

Cooking can destroy up to 40% of Folates in vegetables, and milling and baking can destroy up to 70% in grains and cereals. Folate intake and absorption processes in the small intestine must both function properly to maintain an acceptable Folate status.Folate appears to be absorbed in both the small and large intestines, with a decreasing absorption gradient from the jejunum to the colon. Folate's absorptive pathway may play a vital role in maintaining genetic body homeostasis.[10]

For Example - Steaming rather than boiling, may be promoted as a way to double the folate content of cooked green vegetables, with the cooking water being saved for soups or gravy. These practical strategies have the ability to significantly increase folate intake from natural food sources, as well as play a role in the prevention of folate-related disorders by assisting in the optimization of folate status. [7]

IV. FOLIC ACID FORTIFICATION

Fortification plans have been created internationally with the goal of raising women's FA intakes due to their public health importance. In Spain and the rest of Europe, food fortification with FA is currently voluntary. whereas, according to statistics from the Food Fortification Initiative , more than 60 countries add FA to wheat flour and other cereal products under a required fortification scheme. [2]

A. Folic Acid Fortification of Wheat Flour: Chile Description of Fortification Initiative

Folic Acid fortification of wheat flour was selected as a promising technique for improving Folic Acid intake in the population in Chile by a group of academics and programme planners from the Ministry of Health including experts from the local mill industry for numerous reasons:

1) Wheat flour is a basic meal across the country
2) Milling for bread-making accounts for 90% of total production; additionally, more than 70% of wheat flour is used to make the marraquetas and hallullas, a form of bread popular among Chileans (80 g wheat flour/100 g bread).
3) Mills are technologically advanced and already have quality assurance procedures in place; these characteristics have allowed wheat flour to be fortified with iron as ferrous sulphate (30 mg/kg), thiamine (6.3 mg/kg), riboflavin (1.3 mg/kg), and niacin (13.0 mg/kg) successfully since 1951.The Institute of Public Health monitors quality assurance at the pre-mix vendors and mills on a regular basis
4) The cost of adding Folic Acid to the pre-mix is cheap (about US$ 0.15/tonne of wheat flour), allowing it to be absorbed by the milling industry.

Starting in January 2000, the Chilean Ministry of Health mandated that FA be added to the pre-mix currently used for wheat flour at a concentration of 2.2 mg/kg. This policy, which was adapted to the target group's bread consumption, was predicted to result in a mean extra intake of 400 g/day in women of reproductive age (15 to 44 years)

According to the findings, 98 percent of the women consumed fortified bread on a daily basis, and 89 percent consumed more than 180 mg of Folic Acid per day. The intake of FA enriched wheat flour in Chile is responsible for the increase in blood Folate concentration. As a result, in the population tested, wheat bread fortified with FA was the primary source of this nutrient.

After the programme was implemented, there was a significant rise in serum and red blood cell Folate concentrations, indicating improved Folate intake. These data show that eating an FA-fortified staple food on a daily basis can significantly improve Folate status in women of reproductive age.After 10 months of consuming FA-fortified wheat flour, serum and RBC Folate concentrations increased considerably.[8]

B. Changes in NTD Frequency

Folate consumption has been linked to blood levels of folate, which also appear to be linked to NTD rates. The reduction in NTD rates is the true measure of the impact of increasing Folic Acid use. To assess effectiveness, it was planned to track the prevalence of NTDs following mandated FA fortification to see if the rate fell.

The total number of neural tube defects per 10,000 births is used to compute total prevalence rates.[8]

Table 2. Total NTD Rates before Folic Acid Fortification* (January 1999 to December 2000) and after Fortification† (January 2001 to June 2002) in Santiago, Chile

	Before Fortification	After Fortification	RR (95% CI)	Decline %
NTD rates‡§	17.0	10.1	0.60 (046–0.77)	40

*120,636 births.
†88,538 births.
‡NTD births/10,000 births.
§Live and stillbirths.
NTD = neural tube defects, RR = relative risk, CI = confidence interval.

Use the folate amount (micrograms DFE) to compare against the Recommended Dietary Allowances (RDA) for folate. For women of childbearing age, use the folic acid amount (micrograms) to meet the recommendation for 400 micrograms/day synthetic folic acid for prevention of birth defects.

V. CONCLUSION

Good nutrition is important during pregnancy, by now you've likely read about the importance of taking Folic acid during the pre-pregnancy stage. In the first few weeks of pregnancy, folic acid helps the embryonic neural tube, the precursor to your baby's brain and spinal cord, to properly close. It also assists in the formation of baby's heart and circulatory system and helps lower the chance your baby will have certain birth defects.

Because folic acid is water-soluble, your body isn't able to store an excess amount. Instead, it gets passed through your urine, which is why you need to regularly incorporate enough folic acid into your diet to avoid a deficiency when you're pregnant. Since most birth defects develop in the first few weeks of pregnancy, it's especially important to get enough folic acid as early on as possible.

While not all cases of NTD are preventable by Folic Acid, during a broader analysis of this issue different relevant causes of NTD ought to even be taken under consideration. NTDs are serious and cause life-long disabilities. Fortification of flour and different high-consumption, high-penetration staples with Folic Acid could be a possible, economical, safe, and effective public health policy to prevent NTDs worldwide.

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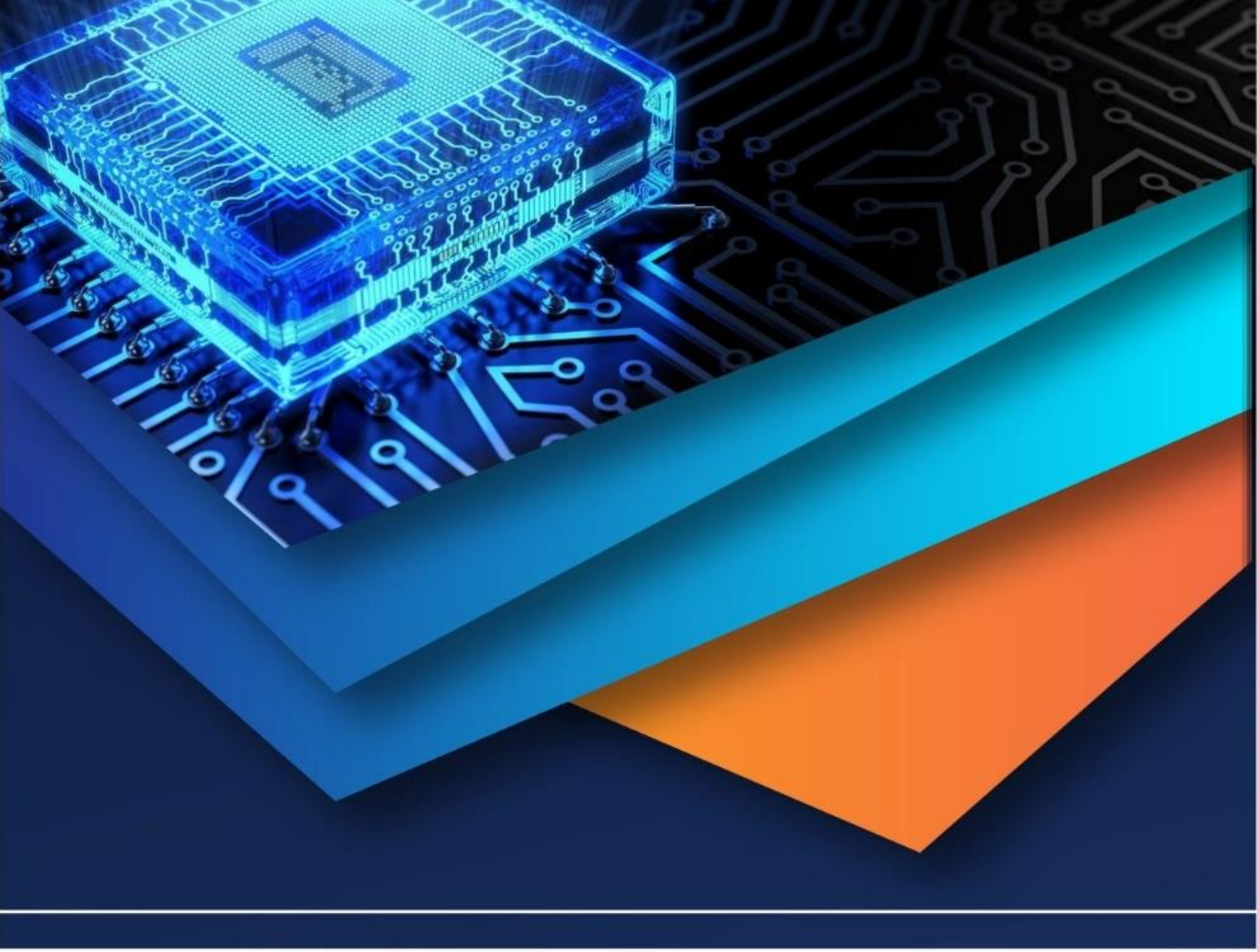

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