

AWARENESS, TIMING, AND TYPE OF PERICONCEPTIONAL FOLATE SUPPLEMENTATION (FOLIC ACID VS L-METHYLFOLATE) AMONG PARENTS OF CHILDREN WITH SPINA BIFIDA: IDENTIFYING GAPS IN PREVENTION STRATEGIES

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ABSTRACT

Background: Periconceptional folate supplementation is an effective strategy for preventing neural tube defects, including spina bifida. However, awareness, correct timing, and knowledge regarding folic acid versus L-methylfolate remain limited in many low-resource settings.

Objective: To assess awareness, timing, and type of periconceptional folate supplementation among parents of children with spina bifida.

Methodology: This analytical cross-sectional study was conducted at Department of Paediatric Neurosurgery, The Children's Hospital Lahore from January 2024 to September 2024, including 137 parents of children with spina bifida. Data were collected using a structured questionnaire regarding awareness of folic acid and L-methylfolate, supplement use, timing, source of information, and barriers. Data were analyzed using SPSS version 26.0.

Results: The mean age of participants was 30.8 ± 5.9 years. Awareness of folic acid was reported by 83 (60.6%) parents, while only 18 (13.1%) had heard of L-methylfolate. Folate supplementation during pregnancy was used by 72 (52.6%) participants, but only 21 (29.2%) started before conception. Folic acid was the most commonly used preparation 58 (80.6%), while L-methylfolate use was reported by only 4 (5.6%). Doctors were the most common source of information 52 (38.0%). Lack of awareness 59 (43.1%) and unplanned pregnancy 42 (30.7%) were the main barriers.

Conclusion: Awareness and timely use of periconceptional folate supplementation were inadequate among parents of children with spina bifida. Preconception counseling and public health education should be strengthened to improve prevention of neural tube defects.

KEYWORDS: Spina bifida; neural tube defects; folic acid; L-methylfolate; periconceptional supplementation

INTRODUCTION

Neural tube defects (NTDs) are serious birth defects caused by failure of the neural tube to close properly during early fetal development (usually before 28 days after conception) [1]. Spina bifida is one of the most common survivable types of NTDs and is linked to long term neurological, orthopedic, urologic and psychosocial issues which can have a profound impact on the quality of life of people with spina bifida [2]. Although prenatal diagnosis and surgical management for spina bifida have improved, it remains a significant public health problem, especially in LMIC, where prevention is not routinely done [3]. Prevention of NTDs by periconceptional folate supplementation is well recognised. A randomized trial has shown that folic acid before pregnancy significantly decreased neural tube defects [4]. More research and systematic reviews have since validated the protective effect of sufficient folate consumption in the periconceptional period on the risk of NTDs, which is about 50–70% [5]. Therefore, the World Health Organization (WHO) and the American College of Obstetricians and Gynecologists (ACOG) have both recommended that women of reproductive age who are planning to get pregnant take folic acid on a regular basis [6][7]. Timing of supplementation is important as many women are not aware of their pregnancy until after their neural tube has closed [8]. Folate should be started preferably before pregnancy and taken during early pregnancy. However, research has demonstrated that many women are not supplementing until after they have confirmed they are pregnant, which is a time they may not be availed of for preventing the disease [9]. Low compliance with folate recommendations is also

due to poor awareness, insufficient preconception counseling, socio-economic factors and a high prevalence of unplanned pregnancies, especially in developing countries [10].

The interest in L-methylfolate, the biologically active form of folate has increased in recent years. L-methylfolate does not need to be converted by MTHFR as does synthetic folic acid, and may have theoretical benefits for people with polymorphisms in the MTHFR gene that disrupt folate metabolism. There has been growing interest in the scientific community about the use of methylfolate supplements, due to emerging evidence, yet awareness and use of this supplement is low among general population [12]. Healthcare providers and patients have been suggested to have inadequate knowledge about the differences between folic acid and folate preparations in their methylated form [13]. Although the burden of neural tube defects in Pakistan is still significant, awareness about periconceptional folate supplementation is low [14]. Lack of public health education, poor counseling prior to pregnancy and poor access to maternal health services are factors that can hinder the ability to take advantage of preventive opportunities [15]. Parents of children with spina bifida can offer an invaluable insight into these gaps, providing a perspective that can help to identify gaps in awareness, timing and use of folate supplementation [16].

Objective

To assess awareness, timing, and type of periconceptional folate supplementation among parents of children with spina bifida.

METHODOLOGY

This was an analytical cross-sectional study conducted at Department of Paediatric Neurosurgery, The Children's Hospital Lahore from January to September 2024, including 137 parents of children diagnosed with spina bifida. The study was designed to assess awareness, timing, and type of periconceptional folate supplementation (folic acid versus L-methylfolate) and to identify gaps in current prevention strategies. Parents or primary caregivers of children with a confirmed diagnosis of spina bifida presenting to the Pediatric Neurosurgery Department during the study period were included. Participants aged 18 years or older who were willing to provide informed consent and complete the study questionnaire were considered eligible. Both mothers and fathers were included if they were directly involved in prenatal healthcare decision-making and were able to recall supplementation practices during the index pregnancy. Parents who declined participation, were unable to provide reliable information regarding folate supplementation during pregnancy, had communication difficulties preventing questionnaire completion, or whose children had other congenital anomalies without spina bifida were excluded from the study. Participants with incomplete questionnaire responses were also excluded from the final analysis.

Data Collection

After obtaining ethical approval from the institutional review board, eligible participants were recruited through consecutive sampling during outpatient and inpatient visits. Data were collected using a structured questionnaire administered through face-to-face interviews. Demographic information included parental age, education level, residence, occupation, and socioeconomic status. Participants were asked whether they had heard of folic acid and L-methylfolate before pregnancy, whether supplementation was used during the index pregnancy, the timing of supplementation (before conception, after conception, or never), and the specific type of folate preparation used (folic acid, L-methylfolate, or unknown). Additional information regarding sources of folate-related knowledge, including doctors, lady health workers, family members, social media, or self-directed learning, was recorded. Participants were also asked to identify barriers that prevented appropriate folate supplementation, including lack of awareness, cost concerns, unplanned pregnancy, limited healthcare access, or other factors. The collected data were entered into a standardized proforma and verified for completeness and accuracy before analysis.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean \pm standard deviation, while categorical variables were presented as frequencies and percentages. Associations between parental characteristics and awareness, timing, and type of folate supplementation were evaluated using chi-square tests or Fisher's exact tests where appropriate. Logistic regression analysis was performed to identify factors associated with appropriate preconception folate use. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of parents was 30.8 ± 5.9 years. Most respondents were mothers 102 (74.5%), while fathers were 35 (25.5%). Urban residents were more common 81 (59.1%) than rural residents 56 (40.9%). Regarding education, secondary education was most frequent 47 (34.3%), followed by graduate or above 38 (27.7%), primary 31 (22.6%), and no formal education 21 (15.3%). Most participants belonged to low socioeconomic status 69 (50.4%), followed by middle 51 (37.2%) and high 17 (12.4%).

Table 1: Demographic Characteristics of Parents of Children with Spina Bifida (n = 137)

Variable	Frequency (n)	Percentage (%)
Age (years), Mean ± SD	30.8 ± 5.9	
Gender		
Mother	102	74.5
Father	35	25.5
Residence		
Urban	81	59.1
Rural	56	40.9
Education Level		
No Formal Education	21	15.3
Primary	31	22.6
Secondary	47	34.3
Graduate or Above	38	27.7
Socioeconomic Status		
Low	69	50.4
Middle	51	37.2
High	17	12.4

Awareness of folic acid was present in 83 (60.6%) parents, while 54 (39.4%) had never heard of it. Awareness of L-methylfolate was much lower, reported by only 18 (13.1%) participants, whereas 119 (86.9%) were unaware of it. Any folate supplement use during pregnancy was reported by 72 (52.6%) parents, while 65 (47.4%) did not use supplementation. Only 39 (28.5%) received preconception counseling, while 98 (71.5%) did not.

Table 2: Awareness and Utilization of Periconceptional Folate Supplementation (n = 137)

Variable	Frequency (n)	Percentage (%)
Heard of Folic Acid	83	60.6
Not Heard of Folic Acid	54	39.4
Heard of L-Methylfolate	18	13.1
Not Heard of L-Methylfolate	119	86.9
Used Any Folate Supplement During Pregnancy	72	52.6
Did Not Use Folate Supplement	65	47.4
Received Preconception Counseling	39	28.5
Did Not Receive Counseling	98	71.5

Among the 72 participants who used folate supplementation, only 21 (29.2%) started it before conception, while most 51 (70.8%) began after conception. Folic acid was the most commonly used preparation, reported by 58 (80.6%) users. L-methylfolate use was very low at 4 (5.6%), while 10 (13.9%) participants did not know the exact preparation used. Supplementation continued for at least the first trimester in 49 (68.1%) cases, whereas 23 (31.9%) used it for a shorter duration.

Table 3: Timing and Type of Folate Supplementation Among Users (n = 72)

Variable	Frequency (n)	Percentage (%)
Timing of Supplementation		
Before Conception	21	29.2
After Conception	51	70.8
Type of Supplement Used		
Folic Acid	58	80.6
L-Methylfolate	4	5.6
Unknown Preparation	10	13.9
Duration ≥ First Trimester	49	68.1
Duration < First Trimester	23	31.9

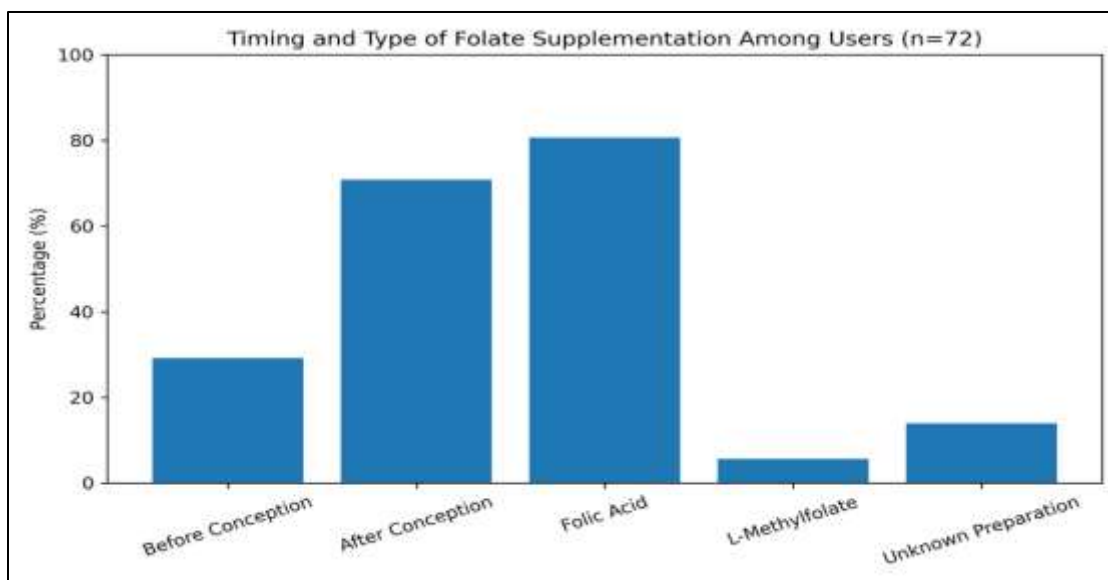


Figure 1. Timing and Type of Folate Supplementation Among Users (n = 72)

Doctors were the most common source of folate-related information, reported by 52 (38.0%) participants, followed by self-knowledge 26 (19.0%), family or friends 24 (17.5%), lady health workers 19 (13.9%), and social media or internet 16 (11.7%). The leading barrier to appropriate folate supplementation was lack of awareness 59 (43.1%), followed by unplanned pregnancy 42 (30.7%), cost concerns 18 (13.1%), limited healthcare access 11 (8.0%), and other reasons 7 (5.1%).

Table 4: Sources of Information and Barriers to Appropriate Folate Supplementation (n = 137)

Variable	Frequency (n)	Percentage (%)
Source of Information*		
Doctor	52	38.0
Lady Health Worker	19	13.9
Family/Friends	24	17.5
Social Media/Internet	16	11.7
Self-Knowledge	26	19.0
Major Barrier		
Lack of Awareness	59	43.1
Unplanned Pregnancy	42	30.7
Cost Concerns	18	13.1
Limited Healthcare Access	11	8.0
Other Reasons	7	5.1

DISCUSSION

The current study measured awareness, timing and form of folate supplementation in parents of children with spina bifida and how much there was to improve in preventive practices. The results indicated poor folic acid awareness and very low knowledge about L-methylfolate, poor preconception counseling and high percentage of folate supplementation after conception. These results indicate that neural tube defects could have been prevented and suggest a need for greater public health action. Sixty six percent of the respondents reported being aware of folic acid, but only 13.1% were aware of L-methylfolate. Awareness about folic acid was quite good but almost two-fifths of Parents remained unaware about the role of folic acid in prevention of neural tube defects. Lack of awareness of methylfolate was especially low suggesting inadequate dissemination of information about newer formulations of folate. Previous studies also show similar results with folic acid awareness between about 40% and 70% and folic acid knowledge significantly lower. Educational status and access to healthcare services were also found in the past to be significant factors in the awareness of folate supplementation, with low education and poor access having significant negative impact [17]. Overall, 52.6% of participants used any folate supplement during pregnancy and almost half of the study participants used no folate supplement. This is of concern given the known benefits of folate on neural tube defects. Folate supplementation rates were also found to be similar in previous studies conducted in developing

countries ranging from 40% to 60%. Adequate health education, antenatal counselling and awareness of the preconception nutrition requirements were cited as reasons for poor supplementation practices in previous studies [18]. One significant finding in this current study was the time of supplementation. Of those who used folate, 29.2% used it prior to conception, while 70.8% used it after conception. Neural tube closure is completed in the first month of fetal development, so if it's delayed, the prevention effect is significantly decreased with folate supplementation. Similar results have been seen in previous studies, in which the majority of women did not start folate supplementation until after the recognition of pregnancy. Results from previous studies have been consistent that the use of folate before conception remains suboptimal and continues to be a significant problem in all NTD prevention programs across the world despite the international recommendations for preconception folate use [19].

The study also highlighted folic acid as the main supplement taken which was used by 80.6% of the participants and L-methylfolate was taken by only 5.6% of the participants. Additionally, 13.9% of participants were not able to describe the formulation they used. The results indicated that there is low awareness and use of methylfolate in normal clinical settings. This finding is consistent with previous studies that also found folic acid to be the most frequently used and prescribed folate supplement. Based on previous studies, scientific interest in methylfolate has grown with the concern of polymorphisms in the MTHFR gene, but its clinical use remains underutilized because of limited awareness, cost and due to a lack of widespread recommendations [20]. Low percentage of preconception counseling (28.5%) was also noted. Over 2/3rds of parents had not been counselled prior to pregnancy. This finding shows gaps in preventive maternal health care services. This finding is similar to previous studies, which report low rates of preconception counseling (usually less than 35%) in low resource settings. Past studies have shown that women receiving counselling from health care professionals were significantly more likely to start folate supplements prior to pregnancy and continue with them throughout early pregnancy [21]. As far as the sources of information, doctors were the first choice for 38.0% of all participants, while self-knowledge was the second choice for 19.0%, followed by family and friends (17.5%) and lady health workers (13.9%), and finally social media (11.7%). The key role of healthcare professionals in raising folate awareness is underscored by this finding. These patterns have been seen in past studies, which found that physicians and healthcare providers were the primary source of information on maternal supplementation. Other studies also found that women who received counseling from health care providers had higher knowledge and better supplementation practices than women who received information from informal sources [22].

Limitations

This study has several limitations that should be considered when interpreting the findings. First, its cross-sectional design limits the ability to establish causal relationships between parental characteristics and folate supplementation practices. Second, the study relied on parental recall regarding supplement use during pregnancy, making the findings susceptible to recall bias, particularly among parents of older children. Third, the study was conducted at a single tertiary-care pediatric neurosurgery center, which may limit the generalizability of the results to the broader population. Fourth, information regarding dosage, adherence, and exact duration of supplementation was not independently verified through medical records or prescription data. Finally, genetic factors such as MTHFR polymorphisms, which may influence folate metabolism and the choice of folate formulation, were not assessed.

CONCLUSION

The present study demonstrated significant gaps in awareness and utilization of periconceptional folate supplementation among parents of children with spina bifida. Although awareness of folic acid was moderate, knowledge regarding L-methylfolate was extremely limited. Most participants who used folate supplementation initiated it after conception rather than during the recommended preconception period, and only a minority received preconception counseling. Lack of awareness and unplanned pregnancies emerged as the major barriers to appropriate supplementation. These findings highlight the need for enhanced public health education, routine preconception counseling, and targeted awareness campaigns to improve timely folate supplementation practices and strengthen neural tube defect prevention strategies.

REFERENCES

1. Baddam S, Khan K, Jialal I. Folic Acid Deficiency. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
2. Commission E. Folic Acid and Neural Tube Defects. Treasure Island (FL): StatPearls Publishing; 2025.
3. CDC. Folic Acid: Facts for Clinicians. Atlanta, Georgia: CDC; 2025.
4. Araszkievicz AF, Jańczak K, Wójcik P, Białecki B, Kubiak S, Szczechowski M, et al. MTHFR gene polymorphisms: a single gene with wide-ranging clinical implications—a review. *Genes*. 2025;16:441.
5. Ou L, Peng L, Wang J, Han C, Zhao X, Wang M, et al. Synergistic effects of MTHFR, MTRR, and MTR gene variants on serum folate levels and cognitive function in Chinese preschoolers: a cross-sectional study. *Nutrients*. 2025;17:2666.

6. Abate BB, Kumsa H, Kibret GA, Wodaynew T, Habtie TE, Kassa M, et al. Preconception folic acid and multivitamin supplementation for the prevention of neural tube defect: an umbrella review of systematic review and meta-analysis. *Neuroepidemiology*. 2024;59:412-425.
7. Sobral AF, Cunha A, Silva V, Gil-Martins E, Silva R, Barbosa DJ. Unveiling the therapeutic potential of folate-dependent one-carbon metabolism in cancer and neurodegeneration. *Int J Mol Sci*. 2024;25:9339.
8. Bo Y, Zhu Y, Tao Y, Li X, Zhai D, Bu Y, et al. Association between folate and health outcomes: an umbrella review of meta-analyses. *Front Public Health*. 2020;8:550753.
9. World Health Organization. *Periconceptional Folic Acid Supplementation to Prevent Neural Tube Defects*. Geneva: World Health Organization; 2023.
10. Tjong E, Dimri M, Mohiuddin S. *Biochemistry, Tetrahydrofolate*. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023.
11. Menezo Y, Elder K, Clement A, Clement P. Folic acid, folinic acid, 5-methyl tetrahydrofolate supplementation for mutations that affect epigenesis through the folate and one-carbon cycles. *Biomolecules*. 2022;12:197.
12. Smith AD, Sobczyńska-Malefora A, Green R, Reynolds EH, Refsum H. Mandatory food fortification with folic acid. *Lancet Glob Health*. 2022;10:e1389.
13. Tinelli C, Di Pino A, Ficulle E, Marcelli S, Feligioni M. Hyperhomocysteinemia as a risk factor and potential nutraceutical target for certain pathologies. *Front Nutr*. 2019;6:49.
14. Janssen JJE, Greffe S, Keijer J, de Boer VCJ. Mito-nuclear communication by mitochondrial metabolites and its regulation by B-vitamins. *Front Physiol*. 2019;10:78.
15. Tourbah A, Gout O, Vighetto A, Deburghraeve V, Pelletier J, Papeix C, et al. MD1003 high-dose pharmaceutical-grade biotin for chronic visual loss related to optic neuritis in multiple sclerosis. *CNS Drugs*. 2018;32:661-672.
16. Lipner SR. Rethinking biotin therapy for hair, nail, and skin disorders. *J Am Acad Dermatol*. 2018;78:1236-1238.
17. Walth CB, Wessman LL, Wipf A, Carina A, Hordinsky MK, Farah RS. Response to: "Rethinking biotin therapy for hair, nail, and skin disorders." *J Am Acad Dermatol*. 2018;79:e121-e124.
18. Ma F, Zhou X, Li Q, Zhao J, Song A, An P, et al. Effects of folic acid and vitamin B12, alone and in combination on cognitive function and inflammatory factors in the elderly with mild cognitive impairment. *Curr Alzheimer Res*. 2019;16:622-632.
19. Ma F, Li Q, Zhou X, Zhao J, Song A, Li W, et al. Effects of folic acid supplementation on cognitive function and Aβ-related biomarkers in mild cognitive impairment. *Eur J Nutr*. 2019;58:345-356.
20. Zhang N, Zhou Z, Chi X, Fan F, Li S, Song Y, et al. Folic acid supplementation for stroke prevention: a systematic review and meta-analysis of 21 randomized clinical trials worldwide. *Clin Nutr*. 2024;43:1706-1716.
21. Gao S, Khalid A, Amini-Salehi E, Radkhah N, Jamilian P, Badpeyma M, et al. Folate supplementation as a beneficial add-on treatment in relieving depressive symptoms: a meta-analysis of meta-analyses. *Food Sci Nutr*. 2024;12:3806-3818.
22. Sarris J, Ravindran A, Yatham LN, Marx W, Rucklidge JJ, McIntyre RS, et al. Clinician guidelines for the treatment of psychiatric disorders with nutraceuticals and phytochemicals. *World J Biol Psychiatry*. 2022;23:424-455.