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Original Article

Evaluating the Hematological Profile of Pregnant Women and the Role of Folic Acid Supplementation in the Third Trimester

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ABSTRACT

Folic acid, the significant vitamin used as supplementation during the third trimester of pregnancy, if not provided in adequate amounts, can lead to chronic diseases. Neural tube development requires folic acid during gastrulation, and its deficiency may lead to the transformation of normal mucosa into a neoplastic condition. **Objectives:** To evaluate the pregnant woman's complete blood count (CBC) during the third trimester of pregnancy. **Methods:** Twenty-four (n=24) females were selected for the study during their third trimester of pregnancy to assess their haematological profiles by taking folic acid as a supplement. A 3-cc blood sample from the median cubital vein was taken from these females, immediately transferred to yellow-capped vacutainers and stored in ice bags. The serum was separated by centrifugation at 1000-2000 rpm for 2 minutes. The supernatant was separated as serum and transferred into vials for diagnostic tests. **Results:** The study suggested that folic acid significantly affects the woman's Complete Blood Count (CBC) profile. In short, folic acid raises the values of CBC during the third trimester. **Conclusions:** Folic acid improves haematological parameters during pregnancy.

INTRODUCTION

Folic acid supplementation has been an essential aspect of prenatal and early pregnancy care worldwide for over two centuries. This is because folic acid supplements have been found to significantly reduce the risk of fetal neural tube defects, which has been a tremendous public health success story in many countries. The incidence of these disorders has decreased significantly after the introduction of food fortification with folic acid [1]. Folic acid supplementation during pregnancy is a widely recognised dietary intervention that protects against neural tube defects and fetal developmental abnormalities. Folate deficiency during conception and pregnancy can lead to abnormal growth, making maternal supplementation a critical step to ensure healthy fetal development [2]. Health authorities recommend folic acid supplementation for conception purposes in all trimesters at the onset of pregnancy [3]. In recent years, there has been significant coverage of the relationship between folic acid supplementation and the risk of neural tube defects (NTDs) and other congenital disabilities sensitive to folic acid. During gastrulation, which occurs in the third week of pregnancy, the dorsal side of the fetus undergoes a remarkable transformation into the neural tube. The neural tube is completely closed by day 28 after conception. Women are given high doses of folic acid to develop the neural tubes to achieve a high serum volume during pregnancy. Researchers have examined the risk of neural tube defects about polymorphisms in the gene methylene

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tetrahydrofolate reductase (MTHFR) [4]. MTHFR genotype, particularly MTHFR TT, influences the risk of neural tube defects by reducing folate concentrations [4]. The role of elevated homocysteine (Hcy) levels and vascular malformations as predictors of pre-eclampsia has been extensively investigated. The primary purpose of the prenatal brain is to control hypertension and prevent pre-eclampsia [5]. The lack of essential food fortification containing folate has raised concerns about cancer risks. Studies have shown that high blood folate levels can lower the risk of colon polyps or cancer. On the other hand, folate deficiency may make normal mucosa more vulnerable to neoplastic transformation [6]. Serum lactic dehydrogenase is involved in adverse drug reactions associated with folate deficiency. According to the findings of Chanarin, Mullen and Anderson in 1958, increased turnover of marrow cells can lead to folate deficiency [7]. Patients with megaloblastic anaemia showed elevated lactate dehydrogenase levels in their plasma [8]. Folate deficiency and excessive supplementation can lead to sudden changes in both mother and offspring's methylome and phenotypic characteristics. Maternal folic acid supplementation has been found to affect the development of asthma, cancer, insulin resistance, autism, and behaviour/attention problems in children. Maternal nutrition plays an important role both before and after birth. Low intake of dietary folate or plasma folate levels during the second trimester of pregnancy usually does not affect birth size. However, low folic acid intake during early pregnancy can hinder fetal brain development and lead to hyperactivity and attention problems in childhood. High levels of maternal plasma folate and serum vitamin B-12 have been associated with the development of atopic dermatitis. Finally, serum lactate dehydrogenase activity can indicate the severity of folate deficiency in haematological diseases, which experienced increased bone marrow activity [9] in pregnant women later in life. Of those who choose to have it, about 5% experience degenerative conditions, such as Crohn's disease. This condition affects folic acid absorption in the ileum, leading to potential complications during pregnancy [4]. Imbalanced folate levels, too low or too high, can cause epigenetic changes that raise concerns about potential effects on the phenotype of both mother and offspring in the short or long term [10]. High folate levels in the blood are associated with a lower risk of colon polyps and cancer. However, when administered in the presence of neoplastic foci, folic acid supplementation may induce colorectal carcinogenesis. In contrast, folate deficiency has an inhibitory effect overall [11].

METHODS

This observational study involved 24 women divided into two groups based on folic acid intake before and during pregnancy. Group A included 10 women who took folic acid regularly during their pregnancy, while Group B included 14 women unaware of the importance of folic acid intake. All participants were evaluated during their third trimester, and their blood samples were analysed using CBC markers to determine desired outcomes.

Table 1: Study design

Groups	No. of Females	Characteristics
Group A	10	Taking folic acid
Group B	14	Not taking folic acid
Total	24	

All participants were requested to sign the consent forms before blood sampling. A 3cc blood sample was taken from the median cubital vein using a 5cc syringe, then transferred immediately to the yellow-capped vacutainers and stored in ice bags. The sample was centrifuged at 1000-2000 rpm for 2 minutes to isolate serum. The supernatant was isolated as serum and then transferred to vials for diagnostic tests. Serum was used to analyse hemolytic profiles, including White Blood Cells (WBCs), Red Blood Cells (RBCs), Platelets (PLT), Hemoglobin (Hb), Hematocrit (HCT), Mean Platelet Volume (MPV), Lymphocytes, and Granulocytes. Sysmex is an automated and computerised haematology analyser designed for in vitro diagnosis of clinical conditions. It can accurately measure 17 haematological parameters like WBCs, RBCs, Hb, HCT, and PLT, making it a valuable tool for clinicians and laboratory professionals. Whole blood component testing has revealed beneficial insights into various disease states, including anaemia, leukaemia, allergic reactions, and viral, bacterial, and parasitic infections. Platelets were electronically assayed and sized using antibody detection. Hematocrit (HCT) was measured as the ratio of total RBC volume to whole blood using joint height detection, while haemoglobin is converted to methemoglobin and read photometrically at 555 nm. Statistical analysis was performed on the data of 24 participants during their 3rd trimester of pregnancy using the independent sample t-test.

RESULTS

A descriptive analysis of WBC levels was observed among the participants. The p-value (0.05) showed significant results for WBC, and the Mean and SEM for WBC of Group B participants came out to be 10.3993 ± 1.09802 while comparing the Group A participants with Group B participants, as given in Table 2.

Table 1: Study design

Parameter	Groups	N	Mean ± SE	p-value
WBC	Group A	10	5.9900 ± 0.21367	0.05
	Group B	14	10.3993 ± 1.09802	

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The value of the Mean and SEM of white blood cells among Group A people came out to be ~6.0000; among Group B people, the value was between 10.0000-12.0000. The p-value (0.05) showed significant results for Group B lymphocytes, as shown in Table 3. The Mean and SEM for lymphocytes were 2.2471±0.49386 while comparing Group A with Group B participants.

Table 3: Independent sample test results for lymphocytes.

Parameter	Groups	N	Mean ± SE	p-value
Lymphocytes	Group A	10	2.2000± 0.00000	0.05
	Group B	14	2.2471±0.49386	

The p-value (0.05) showed significant results for granulocytes in patients. The Mean and SEM for granulocytes for Group B people were 6.7829±0.98279 while comparing Group B with Group A participants as given in Table 4.

Table 4: Independent sample test results for granulocytes

Parameter	Groups	N	Mean ± SE	p-value
Granulocytes	Group A	10	4.6600± 0.00000	0.05
	Group B	14	6.7829±0.98279	

The value of the Mean and SEM of granulocytes for Group A participants ranged between 4.0000-5.0000, and for Group B, the value was between 6.0000-7.0000. The p-value (0.05) showed significant results for RBCs among the participants, as shown in Table 5. The Mean and SEM for GRA was 4.1957±0.10316 for Group B while comparing Group A with Group B participants.

Table 4: Independent sample test results for granulocytes

Parameter	Groups	N	Mean ± SE	p-value
RBC	Group A	10	4.6000± 0.00000	0.05
	Group B	14	4.1957±0.10316	

The value of the Mean and SEM of red blood cells among Group A people was 4.6000, and in Group B, the value came out to be 4.2000. The p-value (0.05) showed significant results for RBC among Group B participants. The Mean and SEM for haemoglobin were 10.7000±0.33725 while comparing Group A with Group B participants, as given in Table 6.

Table 6: Independent sample test results for Haemoglobin

Parameter	Groups	N	Mean ± SE	p-value
Haemoglobin	Group A	10	14.9000± 0.18014	0.05
	Group B	14	1 0.7000±0.33725	

The value of the Mean and SEM of haemoglobin among Group A people ranged between 14.0000- 16.0000, and in Group B, the value was between 10.0000-12.0000.The p-value (0.05) showed significant results for HCT in Group B, as given in Table 7. The Mean and SEM for HCT were 30.4993±1.54082 while comparing Group A with Group B participants.

Table 7: Independent sample test results for HCT

Parameter	Groups	N	Mean ± SE	p-value
HCT	Group A	10	46.8400+ 0.16746	0.05
	Group B	14	30.4993±1.54082	

The Mean and SEM of HCT of Group A people ranged between 40.0000-50.0000; in Group B, the value was 30.0000. The p-value (0.05) showed significant results for PLT in Group B, as shown in Table 8. The Mean and SEM for PLT were 227.0714±18.50615 while comparing the Group A people with Group B participants.

Table 8: Independent sample test results for platelets.

Parameter	Groups	N	Mean ± SE	p-value
Platelets	Group A	10	252.8000 + 7.36025	0.05
	Group B	14	227.0714±18.50615	

The mean and seam of platelets among Group A people was 250.0000; in Group B, the value was between 200.0000-250.0000. The p-value (0.05) showed significant Mean Platelet Volume (MPV) results in Group B people. The Mean and SEM for PLT were 8.5620 + 0.10653 while comparing Group A with Group B.

Table 9: Independent sample test results for mean platelet volume(MPV)

Parameter	Groups	N	Mean ± SE	p-value
Platelets	Group A	10	8.5620 + 0.10653	0.05
	Group B	14	227.0714±18.50615	

The value of Mean and SEM of mean platelet volume among Group A people was between 8.4000-8.6000, and among Group B participants, the value was between 8.4000-8.6000, as given in Table 9.

DISCUSSION

The above investigation was intended to ponder the impact of folic acid on the haematological profile and suggested that folic acid significantly affects the CBC profile [12]. Determination of the blood folate and folic acid status aimed at posting fortification. The results showed a significant effect of folic acid on CBC, reducing the effect of anaemia [13]. Taking folic acid supplements is a common and helpful way to protect against neural tube defects and support fetal development during pregnancy. Ensuring adequate folate levels before and during pregnancy prevents abnormal growth of the child [2]. The WBCs value showed a significant effect of folic acid on CBC. The primary function of folic acid is the formation of red and white blood cells in the body. With typical pregnancy, blood volume grows, causing an affiliated hemodilution. With pregnancy, plasma volume extends furthermore, causing paleness. This outcome physiologically chopped down haemoglobin (Hb), hematocrit (Hct), and RBC values. [14]. Past investigations proposed that genetic and environmental factors added to the aetiology of extreme introvertedness [15]. A previous study discovered 95 of the

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196 participants lacked sufficient haemoglobin response. However, after the Immunofluorescent assay (IFA), the prevalence of anaemia and the low hematocrit value decreased significantly. That study revealed that nearly half of the study participants had a low haemoglobin response, and a large proportion of the anaemia was morphologically atypical of iron deficiency anaemia. Therefore, recognition of anaemia due to etiologies other than iron deficiency is critical in anaemia intervention programs [16]. Folate and vitamin b12 deficiency significantly affect a child's maternal anaemia, so the mother and her offspring's folic acid levels are correlated. Thus, it concluded that it is essential to improve the nutritional value of women at childbearing age to protect their offspring from anaemia [17]. A recent study found that infants born to mothers with prenatal iron deficiency anaemia (IDA) had significantly lower IQs at 12, 18, and 24 months. However, when iron/folic acid supplementation was provided during pregnancy, the mental growth indices of the IDA and non-IDA groups were similar. On the other hand, when folic acid or multiple micronutrients were provided, the mental development index was significantly lower in the prenatal IDA group. These findings suggested that prenatal IDA in the third trimester may adversely affect the child's mental development [18]. A recent study has further emphasised the importance of supplementation during pregnancy in Cameroon due to significant variations in haematological parameters. Additionally, that study provided valuable insight into haematological referrals during pregnancy. The findings also suggested that factors such as being in the third trimester, age 30 to 35 and having a specific blood type may increase the risk of anaemia during pregnancy [19]. In another study, nulliparous pregnant women who received prophylactic iron supplementation had increased oxidative stress and inflammation. In contrast, studies have shown that pregnant women with anaemia benefited from iron supplementation because it improves their haematological status and reduces inflammation without affecting oxidative stress [20]. There was a drastic increase in childhood allergic diseases due to multifactorial aetiology. The developing fetus was highly susceptible to the environment. The gene modules were activated to conserve energy when maternal nutrition is restricted [21].

CONCLUSIONS

Folic acid deficiency significantly affects child and maternal anaemic conditions. The mother and her offspring's folic acid levels are correlated. Thus a deficiency in folic acid supplementation during pregnancy also caused lower Hb levels in the child. So, folic acid supplementation during the third trimester of pregnancy must be appropriately administered with proper awareness of the low-level causing disorders.

Authors Contribution

Conceptualization: KZ, AS, IQ
Methodology: KZ, AS
Formal analysis: KZ, AS
Writing-review and editing: KZ, AS, IQ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Brown ED, Obeng-Gyasi B, Hall JE, Shekhar S. The Thyroid Hormone Axis and Female Reproduction. International Journal of Molecular Sciences. 2023 Jun; 24(12): 9815. doi: 10.3390/ijms24129815.

[2] Lima RP, Do Nascimento RA, Luna RC, Persuhn DC, da Silva AS, da Conceição Rodrigues Gonçalves M, *et al.* Effect of a diet containing folate and hazelnut oil capsule on the methylation level of the ADRB3 gene, lipid profile and oxidative stress in overweight or obese women. Clinical Epigenetics. 2017 Dec; 9: 1-9. doi: 10.1186/s13148-017-0407-6.

[3] Gustot T, Fernandez J, Garcia E, Morando F, Caraceni P, Alessandria C, *et al.* Clinical course of acute-on-chronic liver failure syndrome and effects on prognosis. Hepatology. 2015 Jul; 62(1): 243-52. doi: 10.1002/hep.27849.

[4] Chitayat D, Matsui D, Amitai Y, Kennedy D, Vohra S, Rieder M, *et al.* Folic acid supplementation for pregnant women and those planning pregnancy: 2015 update. The Journal of Clinical Pharmacology. 2016 Feb; 56(2): 170-5. doi: 10.1002/jcph.616.

[5] Jafari-Shobeiri M, Jangi M, Tabrizi AD, Sayyah-Melli M, Mostafa-Gharabaghi P, Ouladsahebmadarek E, *et al.* Diagnostic value of novel biomarker human epididymis protein 4 (HE4) in detecting endometrial cancer: Surgery. 2016; 12:13. doi: 10.15296/ijwhr.2016.07.

[6] Kim YI. Folate and carcinogenesis: evidence, mechanisms, and implications. The Journal of Nutritional Biochemistry. 1999 Feb; 10(2): 66-88. doi: 10.1016/S0955-2863(98)00074-6.

[7] Kremenchuzky S, Hoffbrand AV. Folate deficiency in polycythaemia rubra vera. British Journal of Haematology. 1965 Sep; 11(5): 600-8. doi: 10.1111/j.1365-2141.1965.tb00105.x.

DOI: https://doi.org/10.54393/pbmj.v6i07.910

[8] McCarthy CF, Fraser ID, Read AE. Plasma lactate dehydrogenase in megaloblastic anaemia. Journal of Clinical Pathology. 1966 Jan; 19(1): 51-4. doi: 10.1136/jcp.19.1.51.

[9] Koury MJ and Horne DW. Apoptosis mediates and thymidine prevents erythroblast destruction in folate deficiency anemia. Proceedings of the National Academy of Sciences. 1994 Apr; 91(9): 4067-71. doi: 10.1073/pnas.91.9.4067.

[10] Bekdash RA. Early life nutrition and mental health: the role of DNA methylation. Nutrients. 2021 Sep; 13(9): 3111. doi: 10.3390/nu13093111.

[11] Mortensen JH, Øyen N, Fomina T, Melbye M, Tretli S, Vollset SE, *et al.* Supplemental folic acid in pregnancy and maternal cancer risk. Cancer Epidemiology. 2015 Dec; 39(6): 805-11. doi: 10.1016/j.canep.2015.10.009.

[12] Dam DH, Zhao L, Jelsma SA, Zhao Y, Paller AS. Folic acid functionalized hollow nanoparticles for selective photodynamic therapy of cutaneous squamous cell carcinoma. Materials Chemistry Frontiers. 2019; 3(6): 1113-22. doi:Sim JJ, Lac PT, Liu IL, Meguerditchian SO, Kumar VA, Kujubu DA, *et al.* Vitamin D deficiency and anemia: a cross-sectional study. Annals of Hematology. 2010 May; 89:447-52. doi: 10.1007/s00277-009-0850-3.

[13] Naz R and Ahmad B. Maternal Hemoglobin Value and Other Risking Factors during Pregnancy in Selected Areas of Pakistan 2016-2017. Journal of Applied Environmental and Biological Sciences. 2017; 7(11): 79-87.

[14] Watts DH, Krohn MA, Hillier SL, Eschenbach DA. Randomized trial of antibiotics in addition to tocolytic therapy to treat preterm labor. Infectious Diseases in Obstetrics and Gynecology. 1994 Jan; 1:220-7. doi: 10.1155/S106474499400013X.

[15] Zerbo O, Traglia M, Yoshida C, Heuer LS, Ashwood P, Delorenze GN, *et al.* Maternal mid-pregnancy C-reactive protein and risk of autism spectrum disorders: the early markers for autism study. Translational Psychiatry. 2016 Apr; 6(4): e783-. doi: 10.1038/tp.2016.46.

[16] Belay E, Endrias A, Alem B, Endris K. Hematological responses to iron-folate supplementation and its determinants in pregnant women attending antenatal cares in Mekelle City, Ethiopia. PloS One. 2018 Oct; 13(10): e0204791. doi: 10.1371/journal.pone.0204791.

[17] Zeeshan F, Bari A, Farhan S, Jabeen U, Rathore AW. Correlation between maternal and childhood VitB12, folic acid and ferritin levels. Pakistan Journal of Medical Sciences. 2017 Jan; 33(1): 162. doi: 10.12669/pjms.331.10998.

[18] Chang S, Zeng L, Brouwer ID, Kok FJ, Yan H. Effect of iron deficiency anemia in pregnancy on child mental development in rural China. Pediatrics. 2013 Mar; 131(3): e755-63. doi: 10.1542/peds.2011-3513.

[19] Henri E, Valere MK, Lucas EE, Calixte PI, Ngalame CM, Grâce TT *et al.* Hematological Profile and Risk Factors of Anemia in Pregnant Women: A Cross Sectional Descriptive and Analytical Study in Douala Cameroon. Open Journal of Obstetrics and Gynecology. 2019 Jul; 9(07): 968. doi: 10.4236/ojog.2019.97094.

[20] Rajendran S, Bobby Z, Habeebullah S, Elizabeth Jacob S. Differences in the response to iron supplementation on oxidative stress, inflammation, and hematological parameters in nonanemic and anemic pregnant women. The Journal of Maternal-Fetal & Neonatal Medicine. 2022 Feb; 35(3): 465-71. doi: 10.1080/14767058.2020.1722996.

[21] Bek KM, Nielsen FR, Qvist I, Rasmussen PE, Tobiassen M. C-reactive protein (CRP) and pregnancy. An early indicator of chorioamnionitis. A review. European Journal of Obstetrics & Gynecology and Reproductive Biology. 1990 Apr; 35(1): 29-33. doi: 10.1016/0028-2243(90)90139-R