## **ORIGINAL ARTICLE**

# Folate Levels in Third Trimester of Pregnancy

ZAFAR IQBAL<sup>1</sup>, GHAZIA FATIMA<sup>2</sup>, FAIZ AHMAD FAIZ<sup>3</sup>, HIRA GHAFFAR<sup>4</sup>, SIBGHA NAZ<sup>5</sup>, TAHREEM ANWER<sup>6</sup>

<sup>1</sup>Associate Professor Pathology, Continental Medical College, Lahore

<sup>2</sup>Assistant Professor of Histopathology, Continental Medical College, Lahore

<sup>3</sup>Assistant Professor of Hematology, Islam Medical College, Sialkot <sup>4</sup>Assistant Professor of Microbiology, Continental Medical College, Lahore

<sup>5</sup>Pathology Department, Continental Medical College, Lahore

<sup>6</sup>Senior Demonstrator Pathology, Continental Medical College, Lahore

Correspondence to Dr. Zafar Iqbal, Associate Professor Pathology, Continental Medical College, Lahore

## ABSTRACT

Aim: To determine the folate levels in third trimester of pregnancy

Study design: Cross-sectional study

Place and duration: Conducted at post graduate medical institute, Lahore. Duration was 6 months from June 2022 to December 2022.

**Methods:** Ninety anemic females were selected from the antenatal clinics of different hospitals of Lahore. These incorporated equal numbers of primigravidae and multigravidae and all of them were in the third trimester of pregnancy. They had not taken any hematinic supplements during the pregnancy.

**Results:** Folate deficiency was seen in 44.4% of the primigravidae with peripheral blood macrocytosis and bone marrow megaloblastosis. An association exists between the clinical anemia and the peripheral blood and bone marrow findings with those of serum and red cell folate levels.

**Conclusion:** Folic acid should be included as a routine in hematinic supplements prescribed for pregnant females to protect them from anemia and its consequent complications.

Key words: Folate, gestation, trimester, megaloblastic anemia, macocytosis, bone marrow

## INTRODUCTION

In South India, 54% of the pregnant women had folate deficiency with megaloblastic bone marrow. They were all approaching from low socioeconomic groups of the public<sup>3</sup>.Comparablecause of anemia was distinguished in 62% of the subjects from Zambian inhabitants<sup>4</sup>, 25% in Bantu patients at Johanesburg<sup>2</sup> 26% of the unsupplemented pregnant females in Montreal<sup>5</sup>. Pregnancy is related with confirmation of negative folate balance and folate deficiency. Fall in serum folate levels with quick clearance of intravenously given folate from plasma and proof of megaloblastic marrow change has been observed in a considerable fraction of apparently fit women. It is generally decided that folate requirements during pregnancy exceed the amounts accessible from body stores of folate and other nutritional sources<sup>6</sup>.

There is transport of folate<sup>3</sup> from mother to fetus against the concentration gradient during third trimester of pregnancy representing an energetic placental transport. Amplification of folate stores in this way may well be precious for the infants of very low birth weight<sup>7</sup>. Folate shortage may also be provoked by associated use of drugs<sup>8</sup> and infections, particularly urinary tract infections<sup>9</sup>. Folate deficiency has been seen as an etiological issue in different perinatal complications like abruptio placentae with antepartum bleeding<sup>10</sup>, neural tube defects<sup>11</sup>, premature labor and infant prematurity<sup>12</sup>. This highlights the significance of folic acid as a crucial nutrient throughout pregnancy .The present study was designed to evaluate folic acid status in pregnant females particularly those belonging to less privileged group.

### **METHODOOGY**

A total of one hundred women were selected. They comprised of primigravidae and multigravidae each consisting of 45 subjects and ten non-pregnant controls. The pregnant cases were selected from the antenatal clinics of Lady Willington Hospital, Lady Aitcheson Hospital and Lahore General Hospital, Lahore.

**Inclusion criteria:** The patients selected were in their third trimester of pregnancy, having ages between 18-40 years and they were not taking any drugs which could affect folate concentration.

Received on 05-01-2023 Accepted on 06-03-2023

#### Exclusion criteria:

- 1. H/o skin disease, hyperthyroidism or inflammatory bowel disease.
- 2. Those who have taken folate supplements during the preceding three months
- 3. Hemoglobin level was >11.0 gm./dl.

Bone marrow was aspirated in all the cases from the posterior iliac crest or sternum. The megaloblastic marrows were classified as grade I to IV depending on the severity of the morphological changes. Serum and red cell folate were done by Radio Immunoassay (RIA).

Data was analyzed by SPSS 24.0. Mean±SD was obtained. Chisquare test was done. P-value <0.05 was considered as significant.

### RESULTS

Folate deficiency was found in 20(44.4%) primigravidae and 23(51.1%) multigravidae. Examination of peripheral blood smear revealed marked macrocytosis in 8(17.7%), moderate in 9(20%) and mild in 5(11.1%) of the primigravida group; while in case of multigravidae, it was seen to be marked in 12(26.7%), moderate in 9 (20%) and mild in 4(9.9%) of the patients. Nuclear hypersegmentation of the neutrophils was seen in 14 (31.1%) primigravidae and 12(26.7%) multigravidae. Bone marrow morphology showed grade IV megaloblastic changes in 3(6.8%), grade III in 3(6.8%), grade II changes in 9(20%) and grade I changes in 5(9.9%) of the primigravidae. They were seen to be of grade IV in 2(4.4%), grade III in 5(11.1%), grade II in 8(17.8%) and grade I in 8(17.8%) of multigravidae.

Mean value of serum folate level was  $3.34\pm 1.66$  ng/ml ( $1.4\pm 8.2$  ng/ml) in case of primigravidae and  $3.05\pm 1.19$ ng/ml (1.2 - 5.2 ng/ml) in case of multigravidae .In case of controls the mean value was  $6.67\pm 1.7$ .

Red cell folate level was  $217.01\pm81.25$  mg/ml in case of primigravidae and 165.1151.52 mg/ml in multigravidae. The mean red cell folate was  $414.4\pm120.4$  mg/ml with a range of 280 to 532 mg/ml. The mean values of serum and red cell folate were significantly lower than the control subjects (p<0..01)(Tables 1 and 2).

## **ORIGINAL ARTICLE**

Table 1: Serum folate levels in patients and controls

Folate level (ng/ml)	Primigravidae	Multigravidae	Controls	P value
Mean ± SD	3.34±1.66	3.05±1.19	6.67±1.72	<0.01 (HS)
Ranges	1.4—8.2	1.2—5.2	4.46-9.4	<0.01 (HS)
Total Subjects	45	45	10	

Table 2: Red cell folate levels in patients and controls

Red cell Folate level (ng/ml)	Primigravidae	Multigravidae	Controls	P value
Mean ± SD	217±81.25	165.11±51.52	414.4±120.4	<0.01 (HS)
Ranges	102—435	71—329	4.46—9.4	<0.01 (HS)
Total Subjects	45	45	10	

### DISCUSSION

The patients chosen for the present study were all anemic. They were diagnosed to be folate deficient from peripheral blood and bone marrow morphology. Hypersegmented neutrophils which are exceptional pointer of early folate deficiency<sup>11</sup> were seen in relatively fewer numbers of cases; in 26.7% of primigravidae and 13.1% of the multigravidae with folate deficiency. This may be due to the fact that pregnancy is associated with neutrophilia and a shift to left in the usual lobe count<sup>13</sup>.

Avery and Ledger with similar observations concluded that folic acid supplement was much more reasonable than most of the ingredients of multivitamin preparations. Folic acid deficiency in their observation was the end stage of self-perpetuating cycle of economic and social deficiency, poor nourishment and repeated pregnancies with shortened intervals<sup>14</sup>.

Bone marrow morphology showed that mild to moderate megaloblastic changes (Grade I and II) were seen to be more widespread than the severe forms (Grade III & IV) in both the groups. Karthingiani et al had similar remarks. They found most marked (Grade IV) changes in one case only and milder degree in18 cases<sup>3</sup>.Lowenstein et al<sup>5</sup> also observed similar patterns in their study. Serum and red cell folate levels were considerably decreased from the control values when compared statistically (P<01).

### CONCLUSION

Folic acid should be included as a routine in hematinic supplements prescribed for pregnant females to defend them from anemia and its subsequent complications. **Conflict of interest:** Nil

### REFERENCES

1. Safi, L. Joyeux, G. E. Chalouhi. Periconceptional Folate Deficiency and Implications in Neural Tube Defects. Journal of Pregnancy. Article volume 2012.

- Meselech AD, Ejigu GZ, Shimelash Bite et al. Folic acid usage and associated factors in the prevention of neural tube defects among pregnant women in Ethiopia: cross-sectional study.BMC Pregnancy Childbirth 2017; 17: 313.
- Karthingiani S, Ganausundrum D, Bakar SJ. Megaloblistic erythropoiesis and serum Vitamin B12 and Folic acid levels in pregnancy in south Indian Women . J Obsetet Gynecol Brit Cwlth 2018 : 17: 115-121.
- Edelstein T, Stevens K, Brandt V, Baumslag N, Metz J. Test of folate and vitamin B12 nutrition during pregnancy and the puerperium in a population subsisting on a suboptimal diet. J. Obstet Gynaecol Brit Cwlth 2019; 73: 197-204.
- Lowenstien L, Brunton L. Nutritional anaemia and megaloblastosis in pregnancy. Canad Med Ass J. 1996; 94: 636-654.
- Chanarin I. The megaloblastic anaemia 2<sup>nd</sup> Oxford; Blackwell Scientific Publications 1977; 1-4.
- 7. Keith S. Transfer of folate to the fetus. Developmental Medicine and Child Neurology 1976; 18: 533-538.
- Khursheed M, Karim SM, Rizvi JH, Jaffrey SN, Siddiqui RI. Anaemia in pregnancy – a study of 709 women in Karachi. Trop Doc. 1990; 20: 184-185.
- 9. Wintrobe MM. Clinical Haematology Lea and Febiger, Philaderlphia, 1981; p. 585.
- Fleming Af, Martin JD, Stenhouse NS. The relationship of maternal anemia and folate deficiency to uterine bleeding during pregnancy and fetal malformation. AustNz J Obstet Gynae 1975; 14: 18-24.
- 11. Yates JR. Is disordered folate metabolism the basis for the genetic predisposition to neural tube defects? Clinical Genetics 1987; 31:279-287.
- 12. Lillie EW. Obstetrical aspects of megaloblastic anemia of pregnancy J. Obstet Gynaecol Brit C with 2017;63:736-739.
- Bills T, Spartz L. Neutrophilic hypersegmentation as an indicator of incipient Folic Acid deficiency. Am JC linPath 1977; 68:263-267.
- 14. Avery B, Ledger WJ. Folic acid metabolism in well-nourished pregnant women. Am J Obstet Gynaecol 1970; 4; 616-624.