

*Trop J Obstet Gynaecol, Vol 27 (2), August 2010*

## THE ROLE OF SOME MICRONUTRIENTS (ELDERVIT) IN THE MANAGEMENT OF ANAEMIC PREGNANT NIGERIAN WOMEN: A PRELIMINARY REPORT.

*\*Nwagha UI, \*\*Okeji N, \*\*Clems-Anunwa O, \*\*\*Ejezie FE, \*\*\*\*Nwagha TU and \*\*\*\*\*Iyare E.*

*\*Department of physiology/Obstetrics and Gynaecology, College of Medicine, University of Nigeria.*

*\*\*Department of Obstetrics and Gynaecology, College of Medicine, University of Nigeria Teaching Hospital, Enugu*

*\*\*\*Department of Medical Biochemistry, College of Medicine, University of Nigeria.*

*\*\*\*\*Department of Haematology, College of Medicine, University of Nigeria*

*\*\*\*\*\*Department of Physiology, College of Medicine, University of Nigeria.*

### ABSTRACT

**CONTEXT:** Anaemia continues to be a leading contributor to adverse reproductive outcomes in the developing countries. Although, the commonest cause of anaemia in pregnancy is iron deficiency, the enormous contributions of other micronutrients have been underestimated. As a result, the need to identify relevant micronutrients, which complement iron, in haematopoiesis cannot be over emphasized.

**OBJECTIVES:** To determine the effect of some micronutrients (Cyanocobalamin, {B12} 2500µg, folic acid 0.7mg, niacin 12mg and ascorbic acid 150mg; Eldervit-12) on some haematological parameters of anaemic pregnant women.

**SUBJECTS AND METHODS:** ONE hundred and sixty two (162) anaemic pregnant women aged between 18-38 years were recruited into the study, and randomly divided into two groups. The test group was given two weekly Eldervit-12 injections intramuscularly, and the control group was given placebo (water for injection). Packed cell volume (PCV), reticulocyte count, white cell count and platelet count were estimated before and at the end of the injections using established methods. Student t-test was used to determine test for significance between the groups.

**RESULTS:** The PCV increased significantly from  $25.9 \pm 2.2\%$  and  $26.2 \pm 2.2\%$  to  $37.3\% \pm 2.6\%$  and  $32.4\% \pm 1.9\%$  respectively for test and control ( $P < 0.001$ ). The PCV increase was however, significantly higher in the test when compared with the control ( $P < 0.001$ ). The reticulocyte count also increased significantly from  $2.2\% \pm 0.7\%$  and  $2.3\% \pm 0.7\%$  to  $4.7\% \pm 0.8\%$  and  $2.9\% \pm 0.7\%$  respectively for test and control ( $P < 0.001$ ). But the test showed a more significant increase than the control ( $P < 0.001$ ). There were no significant differences in the WBC and platelet counts ( $P > 0.05$ ).

**CONCLUSION:** Additional micronutrients play a vital role in the management of anaemia in pregnancy. Efforts should be made to qualify and quantify these in order to obtain the actual daily requirements.

**Key words** (Anaemia, Pregnancy, Micronutrients, Haematological parameters.)

### INTRODUCTION

Maternal malnutrition continues to be a significant contributor to adverse reproductive outcomes in developing countries, despite longstanding efforts to fortify foods or distribute medicinal supplements to pregnant women<sup>1</sup>. In the developing world, the majority of women who enter pregnancy are anaemic. Anaemia in these populations is often exacerbated by a high prevalence of infections with intestinal parasites<sup>2,3,4</sup>, malaria and HIV<sup>5</sup> and the occurrence of haemoglobinopathies<sup>6,7,8</sup>.

Iron deficiency anaemia is common in pregnancy, and may be accompanied by other micronutrient deficiencies, because both can result from high rates of infection, diarrhoea, anorexia, poor dietary

quality and nutrient bioavailability<sup>9</sup>. The coexistence of these micronutrient deficiencies and iron deficiency may increase the risk of anaemia and limit the haematological response to iron supplementation<sup>9</sup>. According to Beaton and

#### Correspondence:

**Dr. Uchenna I Nwagha**

**Department of obstetrics and Gynaecology  
University of Nigeria, Enugu Campus.**

**E-mail; [uchenna.nwagha@unn.edu.ng](mailto:uchenna.nwagha@unn.edu.ng);  
[uchenwagha@yahoo.com](mailto:uchenwagha@yahoo.com)**

**Mobile; +234803128233.**

McCabe, 1999, something other than iron may be operating to limit haemoglobin response and anaemia control<sup>10</sup>.

The deleterious effects of anaemia in pregnancy on both mother and child will continue to constitute a burden in our contemporary obstetric practice<sup>11,12</sup>. The incidence is still remarkably high, despite the lower level of normal we have adopted in our own definition<sup>13,14</sup>. There is no doubt that iron deficiency is the commonest cause of anaemia in pregnancy in our environment.<sup>13</sup> However, the enormous contribution of other micronutrients in erythropoiesis cannot be over looked. Studies have shown that despite routine iron supplementation, high incidence of anaemia still exist.<sup>15,16</sup>

This may be as a result of poor compliance, inadequate duration of supplementation of other micronutrients or inadequate treatment of other related factors, low intake of enhancers of iron absorption and high intake of inhibitors of iron absorption such as phytates and oxalates<sup>9</sup>. Several studies have identified multiple micronutrient deficiencies (Vitamins, B12, B2, B6, folate, zinc, ascorbic acid, vitamin E) in association with iron deficiency.<sup>17,18,19</sup> Major physiological changes in pregnancy such as plasma volume expansion which alters blood chemistry and increases maternal to foetal transfer of nutrients, and increased utilization of some of these micronutrients as defense mechanisms against pregnancy induced oxidative stress may be the contributing factors.<sup>20, 21</sup> More recently an analysis of multiple vitamin status of anaemic and non anaemic pregnant women showed a positive correlation between abnormal haematological results and prevalence of vitamin deficiencies. The subjects with iron deficiency anaemia had much higher rates of vitamin C, folate and vitamin B12 deficiencies than the nonanaemic subjects.<sup>22</sup>

In addition to the burden of these nutritional anaemias, malaria parasitaemia is particularly prevalent in our environment,<sup>23,24,25</sup> and contributes significantly in the aetiology of anaemia in pregnancy<sup>26,27,,28,</sup> by causing chronic haemolysis<sup>29,30</sup>. Treatment with iron alone in this circumstance without knowing the serum level may cause over load which could boost the production of free radicals resulting in adverse cellular damage; including the red blood cell.<sup>31</sup>

Few studies have examined the added benefit of multiple micronutrients over iron alone in reducing anaemia and iron deficiency during pregnancy<sup>24</sup>. We

therefore, decided to assess the impact of some of these micronutrients on some haematological profile of anaemic pregnant women who are already on the conventional treatment for anaemia in pregnancy.

## **PATIENTS AND METHODS**

### **Study Design and setting**

This is a single blind, placebo controlled, randomized clinical trial. A total of 162 (one hundred and sixty two) pregnant anaemic patients (PCV <30%) seen, at University of Nigeria Teaching Hospital (UNTH) Enugu, Chukwuasokam maternity Hospital Emene and Kenekchukwu Specialist Hospital Abakpa were recruited for the study. They were aged between 18-38 years and at 18 to 28 weeks gestational age. They were of the same social class and had a minimum of secondary school education. The study lasted from 22<sup>nd</sup> March 2004 to 4<sup>th</sup> October 2004 (7 Months).

Subjects with febrile conditions, multiple pregnancy, preeclampsia, diabetes mellitus, chronic renal disease, sickle Cell anaemia, HIV infections and subjects who dislike injections were excluded from the study. Those whose oral haematinic drug compliance could not be guaranteed were also excluded.

After obtaining ethical approval and informed consent, we consecutively recruited 300 patients that met the above criteria and estimated their PCV. Those with PCV of less than 30 % (162) were selected and randomly divided into two groups using simple random sampling. One hundred and twenty two (122) subjects completed the test (75% compliance), sixty-five (65) test and fifty seven (57) control.

The following haematological indices were measured at the beginning of the test and between 36-38 weeks gestation. Packed cell volume (PCV), reticulocyte count, white cell count and platelet count. PCV was estimated using the microhaematocrit method, reticulocyte count by the supravital staining method, WBC total, by the Turk's solution method, and platelet count by the ammonium oxalate method. The study group was given intramuscular Eldervit- 12 injections (A and B containing Cyanocobalamin, B12, 2500µg, folic acid 0.7mg, niacin 12mg and ascorbic acid 150mg) once every 2 weeks, while the control group was given intramuscular water for injection. Both groups were on conventional treatment with iron. They were also encouraged to continue their normal routine antenatal drugs, (folic acid, multivitamin,

vitamin C, and calcium lactate) at normal dose. They all had anti malaria treatment (intermittent preventive treatment) with sulphadoxine/pyremethamine combination in the second and third trimester.

Values were recorded as mean  $\pm$  standard deviation. Analysis of data was done using spss version 11. Comparison of the mean was by the student paired t-test at 95 %confidence intervals. Values  $\leq 0.05$  were considered as significant.

## RESULTS

The mean age of the subjects was  $30 \pm 4.2$  years while the mean gestational age at recruitment was  $22 \pm 3.1$  weeks. The mean parity was  $3 \pm 1.4$ .

Table I shows that the mean PCV was  $25.9 \pm 2.2\%$  for test and  $26.2 \pm 2.2\%$  for control. This significantly increased to  $37.3 \pm 2.6\%$  and  $32.4 \pm 1.9\%$  respectively ( $P < 0.001$ ). However, comparison of the final value, showed the test group  $37.3 \pm 2.6\%$  was significantly higher than the control  $32.4 \pm 1.9\%$  ( $P < 0.001$ ). In table 2, the mean reticulocyte count was  $2.2 \pm 0.7\%$  and  $2.3 \pm 0.7\%$  respectively for test and control. The test group significantly increased to  $4.7 \pm 0.8\%$ , ( $p < 0.001$ ), and the control also showed a significant increase to  $2.9 \pm 0.7\%$  ( $P < 0.001$ ). However, there was a significant difference in the final treatment values for test  $4.7 \pm 0.8\%$  and control  $2.9 \pm 0.7\%$  ( $p < 0.001$ ). Table 3 shows the total white cell count for test and control before treatment of  $5.4 \pm 1.8 \times 10^9/L$  and  $5.3 \pm 1.8 \times 10^9/L$  respectively, and after treatment of  $5.5 \pm 1.8 \times 10^9/L$  and  $5.7 \pm 1.9 \times 10^9/L$  respectively. Table 4 presents the platelet count for test and control before treatment of  $174 \pm 79 \times 10^3/\mu L$  and  $176 \pm 79 \times 10^3/\mu L$  respectively and after treatment of  $172 \pm 79 \times 10^3/\mu L$  and  $179 \pm 80 \times 10^3/\mu L$  respectively. The results of white cell and platelet counts showed no significant difference ( $p > 0.05$ ).

**Only** 42 subjects from test group and 35 from the control delivered at the various hospitals. There were no significant differences in the Apgar scores  $7.3 \pm 1.2$  for test and  $7.2 \pm 1.2$  for control at one minute, and  $9.4 \pm 1.5$  for test and  $9.3 \pm 1.5$  for control at 5 minutes ( $p > 0.05$ ). The mean birth weights were  $3.84 \pm 0.5$  Kg for test and  $3.82 \pm 0.5$  kg for control respectively and there were no differences noted ( $p > 0.05$ ). There were also no adverse drug reactions recorded. There were no intrauterine foetal deaths, preterm deliveries, congenital abnormalities, or need for new born special care admission in both groups.

## DISCUSSION

In this study, the PCV and reticulocyte count increased significantly in both the test and control subjects. The mean values of PCV and reticulocytes after treatment were however significantly higher in the tests when compared with controls. In a similar study conducted in Nigeria to determine the effect of the same preparation in the prevention of anaemia in pregnancy, the superiority of this additional micronutrient was clearly demonstrated.<sup>35</sup> There were no differences in the white cell and platelet count. A significantly higher reticulocyte count indicates a higher bone marrow activity in the Eldervit group.

Iron deficiency remains the commonest single deficiency leading to anaemia<sup>32</sup>. As a result, in the past pregnant women with anaemia were mainly treated for iron deficiency in most centers using oral iron, or parenteral iron as the case may be. It was not even found necessary to increase the dose of the other hematins.<sup>13</sup> We have thus been able to show that additional micronutrients provide better haematological response than when iron is used alone. Studies have shown that iron deficiency anaemia does not occur in isolation but with associated multivitamin deficiencies.<sup>17,18,19</sup> An isolated study in South East Nigeria found megaloblastic anaemia to be more common than iron deficiency anaemia in pregnant women<sup>33</sup> However, in that study, serum iron, serum ferritin, total iron binding capacity, folic acid and B<sub>12</sub> levels were not determined. Studies have also shown that additional micronutrients had better effect on some haematological indices than when the conventional iron and folic acid was used alone<sup>34,35</sup>.

The contribution of other micronutrients in the aetiology of anaemia in pregnancy has been under estimated. Recent studies have continued to highlight the significant role of other micronutrients in health and disease.<sup>36,37,38,39</sup> Iron deficiency does not occur in isolation, thus all efforts aimed at treatment should include the replacement of other micronutrients. Even if they do not directly stimulate erythropoiesis, they complement the action of iron, may act as antioxidants to prevent free radicals damage and may act as coenzymes in other cellular metabolisms necessary for healthy mother and child. This drug contains an antioxidant micronutrient (ascorbic acid) whose level has been shown to reduce significantly during normal pregnancy<sup>40</sup>. It may have assisted in preventing free radical damage to red blood cell membrane of the

test subjects. However the dose of ascorbic acid in this compound preparation is too small to mop up all the free radicals generated by pregnancy induced oxidative stress.

All the patients were of same social class and were expected to be on average diet. Parental route of administration ensured strict compliance for the test subjects. Prophylactic antimalaria was given to eliminate the significant contribution to anaemia in pregnancy by plasmodium falciparum induced haemolysis. However there was no guarantee that all had good compliance with the oral haematinics. If we had the facilities and resources, it would have been more appropriate to determine the serum levels of the major micronutrients involved in the aetiology of anaemia in pregnancy. This will enable us determine the actual daily dose required during pregnancy. We had no facilities for electronic counting for white cell and platelet count and that could have resulted in our inability to reach any conclusion on these parameters. Although the highest degree of professionalism in this study, a double blind placebo controlled randomized clinical trial would have been more appropriate to completely eliminate micro elements of bias. There were no adverse drug reactions as the drugs are water soluble vitamins and toxicity is rare.

Malaria, as a significant contributor to anaemia in pregnancy in our environment does not lead to iron depletion. It is thus important, if facilities are available to determine the serum levels of iron in these patients in other to prevent iron over load. Alternatively, studies should be conducted using reduced amounts of iron and increased amount of other micronutrients. Further studies should also include the determination of actual levels of these micronutrients in pregnancy so as to quantify the daily amount needed for replacement therapy.

**ACKNOWLEDGEMENTS:**

We wish to thank staffs of the antenatal clinic of UNTH, Kenechukwu and Chukwuasokam hospitals. We are immensely grateful to ELBE Pharmaceuticals LTD for their financial assistance

**TABLE 1: MEAN PCV VALUES .**

	PCV Values (%)	T-test	P-Value
Test(n=65)	BT=25.9±2.2	27.14	P<0.001
	AT=37.3±2.6		
Control (n=57)	BT=26.2±2.2	16.31	P<0.001
	AT=32.4±1.9		
TestvsControl(AT)	Test=37.3±2.6	12.25	P<0.001
	Control=32.4±1.9		

(BT=before treatment, AT After treatment).

**TABLE 2: Mean reticulocytes values (%)**

	Reticulocytes (%)	T-test	P-value
Test(n=65)	BT= 2.2±0.7	14.7	P<0.001
	AT= 4.7±0.8		
Control (n=57)	BT=2.3±0.7	3.75	P<0.05
	AT= 2.9±0.7		
Test/Control(AT)	Test=4.7±0.8	9.0	P<0.001
	Control=2.9±0.7		

(BT=before treatment, AT After treatment).

**TABLE 3: MEAN WHITE CELL COUNT ( 10<sup>9</sup>/L)**

	WBC(10 <sup>9</sup> /L)	T-test	P-value
Test(n=65)	BT=5.4±1.8	0.25	P>0.05
	AT=5.5±1.8		
Control (n=57)	BT=5.3±1.8	0.9	P>0.05
	AT=5.7±1.9		
Test/Control(AT)	Test=5.5±1.8	0.57	P>0.05
	<b>Control=5.7±1.9</b>		

(BT=before treatment, AT After treatment).

**TABLE 4: MEAN PLATELET COUNT (10<sup>3</sup>/μL)**

	Platelet count(10 <sup>3</sup> / μL)	T-test	P-value
Test(n=65)	BT=174±79	0.11	P>0.05
	AT=172±79		
Control (n=57)	BT=176±79	0.16	P>0.05
	AT=179±80		
Test/Control(AT)	Test=172±79	0.38	P>0.05
	Control=179±80		

**Values as mean ± standard deviation.**

(BT=before treatment, AT After treatment).



**REFERENCES**

1. Makola D, Ash DM, Tatala SR, Latham MC, Ndossi G, Mehansho H. A Micronutrient Fortified Beverage Prevents Iron Deficiency, Reduces Anemia and Improves the Hemoglobin Concentration of Pregnant Tanzanian Women. *J Nutr* 2003; 133: 1339-46.
2. Van Den Broek N. Anaemia in pregnancy in developing countries. *Br J Obstet Gynaecol* 1998; 105: 385-90.
3. Fleming AF. Iron status of anaemic pregnant Nigerians. *J Obstet Gynaecol Br Common* 1969; 76: 1013-17.
4. Suhamo D, West CE, Muhilal KD, Hautvast JG AJ. Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia. *Lancet* 1993; 342: 1325-28.
5. Van Den Broek NR, White SA, Neilson JP. The relationship between asymptomatic human immunodeficiency virus infection and the prevalence and severity of anemia in pregnant Malawian women. *Am J Trop Med Hyg* 1998; 59: 1004-7.
6. Rush D. Nutrition and maternal mortality in the developing world. *Am J Clin Nutr* 2000; 72: 212S-240S.
7. Ratten GJ and Beischer NA. The significance of anaemia in an obstetric population in Australia. *J Obstet Gynaecol Br Common* 1972; 79: 228-37.
8. Harrison KA and Ibeziako PA. Maternal anaemia and fetal birth weight. *J Obstet Gynaecol Br Common* 1973; 80: 798-804.
9. Allen LH, Rosado JL, Casterline JE, Lopez P, Munoz E, Garcia OP, Martinez H. Lack of hemoglobin response to iron supplementation in anemic Mexican preschools with multiple micronutrient deficiencies. *Am J Clin Nutr* 2000; 71: 1485-94.
10. Beaton GH, McCabe GP. Efficacy of intermittent iron supplementation in the control of iron deficiency anaemia in developing countries: an analysis of experience. Toronto: The Micronutrient Initiative, 1999.
11. Marchant T, Schellenberg JA, Nathan R, Abdulla S, Mukasa O, Mschinda H, et al. Anaemia in pregnancy and infant mortality in Tanzania. *Trop Med Int Health* 2004; 9(2): 262-6.
12. Brabin B, Prinsen - Geerlings P, Verhoeff F, Kazembe P. Anaemia prevention for reduction of mortality in mothers and children. *Trans R Soc Trop Med Hyg* 2003; 97(1): 36-8.
13. Ogunbode O. Management of anaemia in pregnancy. *Nig Med Pract* 1984; 8(5/6): 105-7.
14. Ogunbode O. Anaemia in pregnancy. In Ogunbode T (ed). *Medical disorders in Tropical obstetrics*. Ibadan, Evans Brothers 1997; 1-20.
15. Simmons WK. Control of iron and other micronutrient Deficiencies in English speaking Caribbean. *Bull Pan Am Health Organ* 1994; 28(4): 302-11.
16. Okafor LA, Diejomaoh FM, Orosaye AU. Bone marrow Status of anaemic pregnant women on supplemental iron and folic acid in a Nigerian Community. *Angiology* 1985; 36(8): 500-3.
17. AcKurt F, Wetherrilt H, Loker M, Hacibekiroglu M. Biochemical assessment of nutritional status in pre and postnatal Turkish women and Outcome of pregnancy. *Eur J Clin Nutr* 1995; 49(8): 613-22.
18. Knight Em, Spurlock BG, Edwards CH, Johnson AA, Oyemade UJ, Cole OJ, et al. Biochemical Profile of African American women during three trimesters of pregnancy and at delivery. *J Nutr* 1994; 124: 943S-53S.
19. Pardo J, Peled Y, Bar J, Hod M, Sela BA, Rafel ZB, et al. Evaluation of low serum B(12) in the non anaemic pregnant patients. *Hum Reprod* 2000; 15(1): 224-6.
20. Dejmeck J, Ginter E, Solansky I, Podrazilova K, Benes I, Sram RJ. Vitamin C, E, and A levels in Maternal and fetal blood for Czech and Gypsy ethnic group in the Czech Republic. *Int J vitam Res.* 2002; 72(3): 183-90.
21. Pressman EK, Cavanagh JL, Mingione M, Norkus EP, Woods JR. Effects of maternal antioxidants supplementation on Maternal and fetal antioxidant levels: a randomized double blind study. *Am J Obstet Gynecol* 2003; 189(6): 1720-5.
22. Ma AG, Chen XC, Wang Y, Xu RX, Zheng MC, LI JS. The multiple vitamin status of Chinese pregnant women with anaemia and non anaemia in the last trimester. *J Nutr Sci Vitaminol* 2004; 50(2): 87-92.
23. Chukwura EI, Okpala EE, Ani IQ. The prevalence of Malaria parasites in pregnant women and other patients in Awka Urban, Anambra State Nigeria. *Journal of Biomedical Investigation* 2003; 1: 48-52.
24. Anorlu RI, Odum CU, Essien EE. Asymptomatic malaria parasitaemia in pregnant women at booking in a primary health care facility in a peri urban community in Lagos, Nigeria. *Afr Med*

- Med Sci 2001; 30: 39-41.
25. Bouyou- Akotet MK, Lonete-Collard DE, MabikKa- anfoumbi M, Kendjo E, Matsiegui PB, Mavoungou E, *et al.* Prevalence of Plasmodium falciparum infection in pregnant women in Gabon. *Malar J* 2003; 2(1): 18-24.
  26. Egwunyenga AO, Ajayi JA, Nmorsi OP, Duhlinka-Popova DD. Plasmodium/Intestinal helminth co Infections among pregnant Nigerian women. *Mern Inst Oswaldo Cruz* .2001; 96(8); 1055-9.
  27. Dicko A, Mantel C, Thera MA, Doumbia S, Diallo M, Diakite M, *etal.* Risk factor for malaria infection and anaemia for pregnant women in the Sahel area of Bandigara, Mali. *Acta Trop* 2003; 89(1): 17-23.
  28. Egwunyenga OA, Ajayi JA, Duhlinka – Popova DD. Malaria in pregnancy in Nigerians: Seasonality and relationship to splenomegaly and anaemia. *Indian J Malariol* 1997; 34(1): 17-24.
  29. Shulman EE, Dorman EK. Importance of prevention of malaria in pregnancy. *Trans R Soc Trop Med Hyg* 2003; 97(1): 30-5.
  30. Brabin BJ, Prinsen-Gearlings PD, Verhoeff FH, Fletcher KA, Chimsuku LH, Ngwira BM, *et al.* Haematological profile of people of rural Southern Malawi; an overview. *Ann Trop Med Parasitol*. 2004; 98(1) 71-83.
  31. Lachili B, Hininger I, Faure H, Arnaud J, Richard MJ, Favier A *et al.* Increased lipid peroxidation in pregnant women after iron and vitamin C supplementation. *Biol Trace Elem Res* 2001; 83(2): 103-10.
  32. Omigbodun OA. Recent Trends in the Management of Anaemia in pregnancy. *Trop J Obstet Gynaecol* 2004; 21(1): 1-2.
  33. Obi GO, Chukwudebelu WO. The iron status of anaemic Pregnant Igbo women In Nigeria: *Trop Geogr Med* 1981; 33(2): 27-33.
  34. Ajayi GO, Fadiran EO. The Effect of 61 days of combined Iron (Chemiron) and single iron therapy on haemoglobin, packed cell volume, platelets and reticulocytes during pregnancy; a preliminary report. *Clin Exp Obstet Gynecol*.1998; 25(3): 107-11.
  35. Feyi-Nwagboso PA, Aluka C, Nwaogu CG, Archibong EI, Ejikeme EC. The Role of Parenteral Multivitamin Preparation (Eldervit) in the Prevention Of Anaemia in Pregnancy. *Trop J Obstet Gynaecol* 2005; 22(1): 159-163.
  36. Shah D, Sachdev HP. Maternal Micronutrients and fetal Outcome. *Indian J Pediatr* 2004; 71(11): 985-90.
  37. Black RE. Micronutrients in pregnancy. *Br J Nutri* 2001; 85: S193-7.
  38. Gross R, Solomon NW. Multiple micronutrient deficiencies: Future research needs. *Food Nutr Bull* 2003; 24: 542-53.
  39. Ramakrishnan U. Prevalence of micronutrient malnutrition worldwide. *Nutr Rev* 2002; 60: 546-52.
  40. Ejezie EE, Onwusi EA, Nwagha IU. Some Biochemical Markers of Oxidative Stress in Pregnant Nigerian Women. *Trop J Obstet Gynaecol* 2004; 21: 122-4.