INTERNATIONAL JOURNAL FOR INNOVATIVE RESEARCH IN MULTIDISCIPLINARY FIELD ISSN: 2455-0620 Volume - 6, Issue - 6, June – 2020
Monthly, Peer-Reviewed, Refereed, Indexed Journal with IC Value: 86.87 Impact Factor: 6.497
Received Date: 30/05/2020 Acceptance Date: 16/06/2020 Publication Date: 30/06/2020

A Study of trace elements (Copper, Zinc and Iron) status in anaemic pregnant women in Waghodia, Vadodara

[1]Neha Sheth , [2] Ivvala Anand Shaker
[1]Tutor,[2] Professor & Head , Department of Biochemistry, Parul Institute of Medical Sciences and Research, Parul University, Waghodia, Vadodara, Gujarat - India.
Email – [1] nehasheth2487@gmail.com, [2] anandshaker@rediffmail.com

Abstract: *Aim of this study was to evaluate the tract elements (Copper, Zinc and Iron) status in anaemic pregnant women. This was a cross sectional study that comprised of 80 individuals of which 40 were cases and 40 healthy controls. On the basis of clinical history, laboratory investigation and other demographic parameter by pre-tested semi structured questionnaire diagnosis of anaemia was made in pregnant cases. Serum Copper, Zinc and Iron were measured in all the individuals. Levels of S. Copper were significantly higher [median: 251.44µg/dl Vs. 180.55µg/dl], S. Zinc [median:33.33µg/dl Vs. 48.87µg/dl] and S. Iron [median: 30.94µg/dl vs.52.62µg/dl] were significantly lower in anaemic pregnant women as compared to non-anaemic pregnant women respectively. While correlating with haemoglobin S. Copper showed moderate negative correlation; S. Zinc showed mild positive correlation and S. Iron showed moderate positive correlation. It was concluded that evaluation of trace elements may be useful tools for risk micronutrients deficiency during pregnancy and can be used together with better accuracy diagnosis of nutritional anaemia.*

Key Words: *Anaemia, pregnancy, traces elements (Copper, Zinc and Iron).*

1. INTRODUCTION:

Pregnancy is a phase of increased metabolic demands, mainly due to alteration in the woman's physiology and requirements of growing fetus (1). These leads to physiological modification, during pregnancy which involves haematological changes result in increased plasma volume and red blood cells, while biochemical or metabolic changes results in decreased concentrations of circulating nutrient-binding proteins, increase in a requirement of calories as well as some alteration is seen for vitamins and minerals, collectively referred as micronutrients, which had remarkable influence on the health of pregnant women and growing fetus (2). These can lead to disastrous consequences for both mothers and new born infants, when such physiological change is aggravated by under nutrition and leads to micronutrient deficiency states, such as anaemia and is more prone in emerging countries like India (3,4).

The WHO estimated that more than 50% of all women living in developing countries are anaemic. While in India, Gujarat National Family Health Survey – 4 in 2015-16 shows that 54% of women in rural and 47 % women in urban areas are anaemic during pregnancy (5). The survey of severity of anaemia says that, about 40% of women are mildly anaemic, 12% are moderately anaemic, and 1% is severely anaemic. Medical Practitioner believes that provision of iron and folic acid supplements in health programmes will not solve the problem of anaemia. Since large span of time has passed, the problem is still question to be solved, which needs total elimination.

Anaemia is a condition of low concentration of circulating Haemoglobin (Hb) where concentration falls below the threshold and lack of functioning RBCs that leads to insufficient oxygen-carrying capability; causing unusual complication (6). It can affect at any age and either gender, in spite of the fact, it is more prevalent in pregnant women and young children. It contributes to 20% of deaths among pregnant women (7,8). This paper discusses about the minerals (i.e. trace elements) in pregnancy—their status and consequences of their deficiency.

2. LITERATURE REVIEW:

Trace elements concentrations during pregnancy alters because the expansion of red blood cell mass is proportionally less than that of plasma, some biochemical variable for trace elements, fall in parallel to red blood cell volume.

Iron most abundant trace element in our body and plays an important role in heme metabolism. Deficiency of iron stores results in anaemia, which may increase the risk of death from haemorrhage during delivery, affect pregnancy, foetal development, and childbirth. One of most common cause of nutritional anaemia is deficiency of iron stores and at some instances; it gets aggravated by dietary contents leads poor absorption of iron. For example, rural diets are rich in phytates and phenolic compounds prevent absorption of iron, thereby contributing to the anaemic condition (9,10).

There are the evidences suggest that iron deficiency causes poor cognitive, motor, neurophysiological, and socio-emotional development of children. Anaemic mothers give birth to neonates with suboptimal iron stores and are at high risk of developing iron deficiency anaemia (11). It has been said that, iron deficiency is the most prevalent cause of anaemia, but only rarely does iron deficiency exist by itself. Individuals who are deficient in only one trace element i.e. iron are also deficient in other important micronutrients, although this important correlation is often overlooked by the medical profession and almost always unthought-of by the public at large (12).

Zinc is second vital trace element. It is involved in various biochemical functions of the body, i.e. acting as structural element of several proteins such as growth factors, cytokines, receptors, transcription factors, co-factor for various enzymes, DNA and RNA which plays an in the cellular signalling pathways and emphasizing its importance during periods of gestation and foetal life (13).

Copper, third essential trace element found, and is biologically involved in building connective tissues, iron metabolism, production of melatonin, immune system function and development of the central nervous system (14). It is a vital cofactor of antioxidant enzymes, functioning act as antioxidant defence system. These enzymes are expressed in mother and foetus tissues and play a vital role in removing pregnancy oxidative stress. In absence of this protective mechanism, oxidative stress may lead to poor pregnancy outcomes such as pre-eclampsia, foetal growth restriction, and abortion (3,15). Copper deficiency is rare, but cases have been identified in humans, which manifested as neutropenia, anemia and skeletal abnormalities with atherogenic and electrocardiographic irregularities and are linked to low birth weight of neonates (16). During pregnancy, the metabolism of copper and iron is tightly interlinked. Deficiency of one has marked effects on the metabolism of the other metal (11).

The trace elements deficiency (i.e. iron, zinc and copper) is associated with anaemia and affects foetal growth and women during pregnancy in under nutrition condition. Thus, Pregnancy is associated with increased demand of all the nutrients like Iron, Copper, Zinc etc. in anaemic condition need to studied.

3. MATERIALS:

The study was carried out among pregnant women who approached antenatal clinic at the Department of Obstetrics and Gynaecology of the Parul Sevasharam Hospital and Parul Institute of Medical Sciences and Research (PIMSR).

3.1 Duration of the Study: 7 months

3.2 Study Design: Hospital based cross sectional study.

3.3 Source of data: Eighty Pregnant women of aged 20 to 35 years were inquired about her obstetric profile, socio-economic status, and other demographic parameters by utilizing a pre-tested semi structured questionnaire. The gestational age of the women was calculated by inquiring about the last menstrual period of the women. The objectives of the study were explained to the women and informed consent was obtained.

The study will be carried out among two groups.

1) Group I: Control (n=40): Non-Anaemic pregnant women having (Hb higher than 11.0 g/dL)
2) Group II - Subjects (n=40): Anaemic pregnant women (Hb lower than 11.0 g/dL)

And, further this group had been divided into Mild, Moderate, and Severe anaemia on the basis of following (Table 1).

Table 1-- Categorization of anaemia according to WHO (17).

Category	Anemia Severity	Haemoglobin level (g/dl)
1	Mild	10.0-10.9
2	Moderate	7.0 – 9.9
3	Severe	Less than 7.0

The following inclusion and exclusion criteria were adopted:

Inclusion criteria:

Pregnant women with second and third trimester were included in study.

Exclusion criteria:

Pregnant women with hypertension, diabetes mellitus, tuberculosis, cardiovascular disease, respiratory problem, liver disease, renal disease and metabolic disorders were excluded from the study.

4. METHOD:

The samples were collected from collection centre and analysed at Clinical Chemistry Laboratory of Biochemistry Department of PIMSR and PSH Hospital, Waghodia, Vadodara. Venous samples (2ml) were collected in plain vacutainer. Blood samples was allowed to clot at room temperature and then centrifuged at 3000 rpm for 5 minutes.

Samples were stored at 2-8°c until analysis. Following investigations was estimated by UV-vis Spectrophotometer by following methods: Serum Iron (18), Serum Zinc (19) and Serum Copper (20).

4.1 Statistical analysis:

All data analysis was done using Microsoft Excel and the Statistical software MedCalC version 11.5.0. Mean ± Standard deviation calculated. Results were analysed statistically for significance by Independent's' test, Box plot for detailing and Pearson correlation 'r' test (correlation coefficient test) was done to assess the relation of trace elements.

4.2 Ethical consideration:

The protocol for this study was approved by the Institutional Ethics and Research Committee (IERC) of Parul Institute of Medical Sciences and Research (PIMSR) in accordance with the ethical standards of the committee on human institutional experimentation and with the Helsinki Declaration of 1975 that was revised in 2000.

5. RESULT & ANALYSIS:

In present study of trace elements, comparison was done between pregnant women with anaemia to non-anaemic pregnant women of same gestational period, following observations were noted (Table 2).

Table 2 -- No. of participants in each group

Group I (Control) (Non-Anaemic pregnant women)	Group II (Subjects) (Anaemic pregnant women)		
	Mild	Moderate	Severe
40	14	25	01

The Box and whisker plot show the comparison of trace elements levels between Control (Non-anaemic Pregnant women) group and Case (Anaemic Pregnant women) group. The comparison of Serum Copper in Control and Case group having median value 180.55µg/dl and 251.44µg/dl respectively (Fig. 1). The comparison of Serum Iron in Control and Case group having median value 52.62µg/dl and 30.94µg/dl respectively (Fig. 2). The comparison of Serum Zinc in Control and Case group having median value 48.87µg/dl and 33.33µg/dl respectively (Fig. 3).

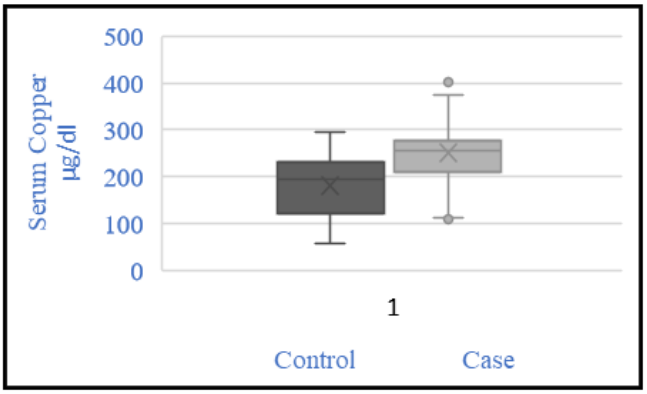

Fig. 1- Comparison of Serum Copper (µg/dl) between Non-anaemic Pregnant women & Anaemic Pregnant women

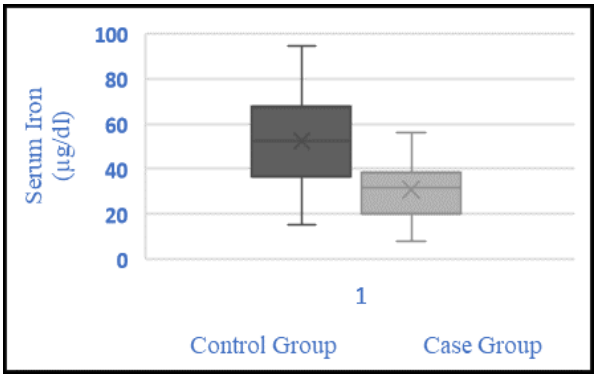

Fig. 2 - Comparison of Serum Iron (µg/dl) between Non-anaemic Pregnant women & Anaemic Pregnant women

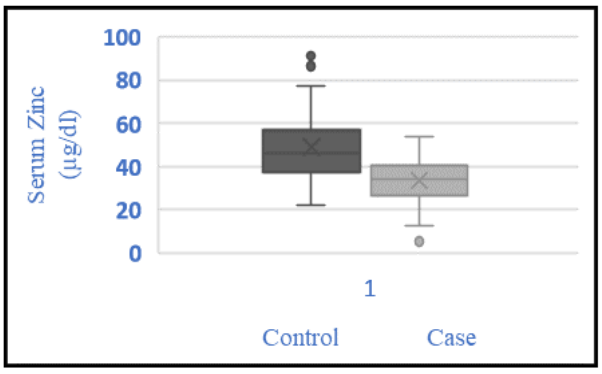

Fig. 3 - Comparison of Serum Zinc (µg/dl) between Non-anaemic Pregnant women & Anaemic Pregnant women

Statistical comparison of trace elements between anaemic and non-anaemic pregnancy women of 2nd and 3rd trimester indicates that significantly reduction (P<0.001) of Serum Iron and Serum Zinc, while Serum Copper was significantly increased (P<0.001) results was observed (Table 3).

Table 3-- Comparison of biochemical Variables (Trace Elements) Levels between Anaemic and Non- Anaemic Pregnant women[1]

Variables	Reference Range	Non-Anaemic (n= 40)	Anaemic (n= 40)	p- Values
Iron	50-170 µg/dl	52.62±20.52	30.94±12.56	p<0.0001
Zinc	70-125 µg/dl	48.87±14.96	33.33±11.28	p<0.0001
Copper	63-140 µg/dl	180.55±63.59	251.44±72.85	p<0.0001
Values are expressed as mean ± standard deviation *p-Values Statistically significant (p < 0.05); highly significant (p<0.0001)				

The moderate negative correlation of Serum Copper with haemoglobin is observed (Fig. 4); moderate positive correlation of Serum Iron with haemoglobin is observed (Fig. 5); mild positive correlation of Serum Zinc with haemoglobin (Fig. 6) in anaemic pregnant women. Serum iron showed a decreasing trend as haemoglobin decreased (Fig. 5); while an inverse correlation was found between copper and haemoglobin levels (Fig. 4).

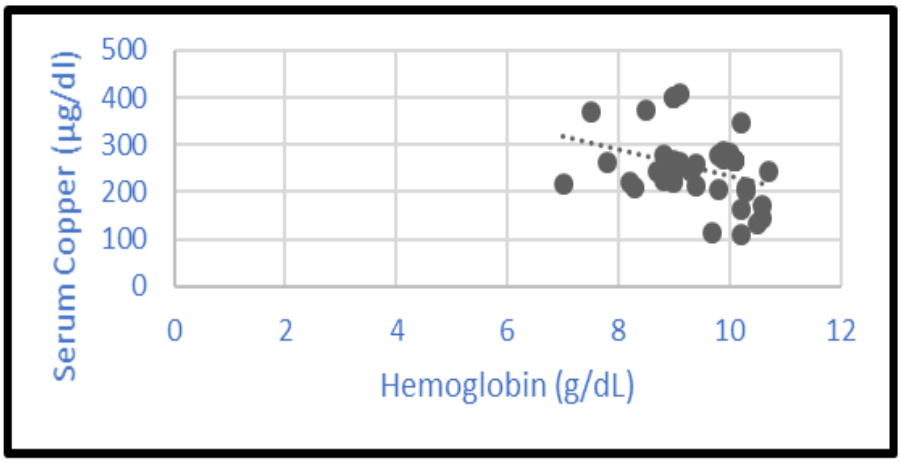

Fig. 4- Correlation between Hemoglobin and Serum Copper (µg/dl) in anemic pregnant women
n= 40; r= -0.343

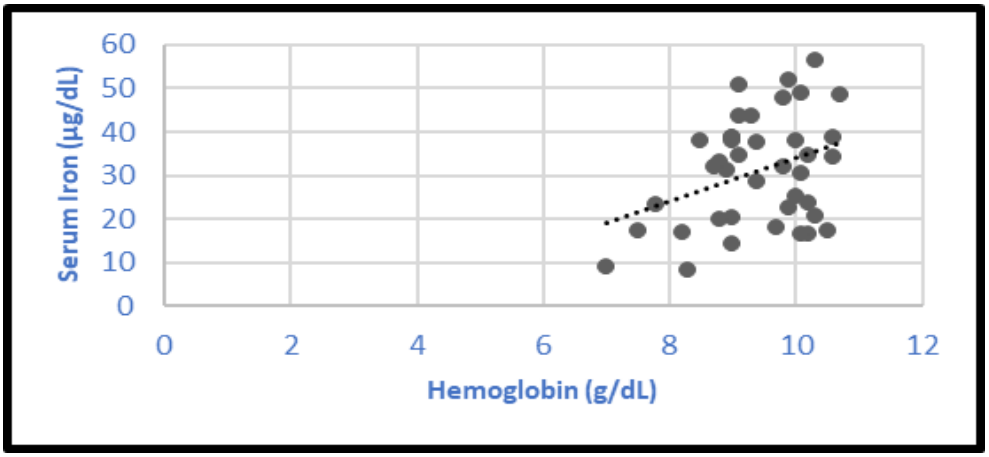

Fig. 5 - Correlation between Hemoglobin and Serum Iron (µg/dl) in anemic pregnant women
n= 40; r= 0.352

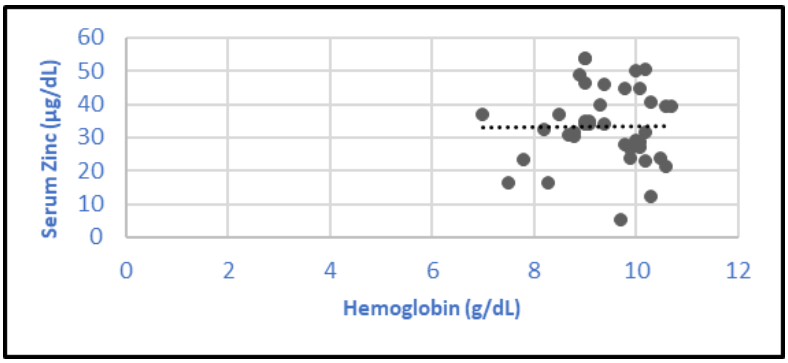

Fig. 6 - Correlation between Hemoglobin and Serum Zinc (µg/dl) in anemic pregnant women
n= 40; r= 0.013

6. DISCUSSION:

Micronutrients are essential for normal function, growth and development and have important effects on the health of the mother and fetus. But biological mechanisms of these minerals are not completely understood. During pregnancy, increased physiological changes to support body metabolism in the mother and growing foetus lead to an increased need for micronutrients and excessively depleted. Deficiency of these trace elements can lead to anemia, hypertension, obstetric complications and even maternal death and in fetus lead to a fail in growth and development.

The present study was undertaken in a community, which consumed a diet where the main source of energy was cereals. The presence of higher amount of phytates and dietary fibre in such diet, known to cause poor zinc absorption could be a major contributing factor for high prevalence of zinc deficiency in our study population. Poor pre-pregnancy nutritional status and low serum zinc levels could be other contributing factors leading to low serum zinc levels during pregnancy with anaemia resulting from low dietary bioavailability (3).

Pregnant women had significantly elevated serum copper levels and the levels had further increased in pregnant women with anemia. The increase in copper in anemic women could be a compensatory mechanism to counteract anemia and this is accompanied by increased synthesis of ceruloplasmin which has ferroxidase like activity (16,21).

Most of the vegetarian diet, composed almost entirely of cereals is consumed with excess of inhibitors of iron absorption (phytates); thus, resulting from poor dietary iron bioavailability causes anaemia and has been associated with maternal mortality (1).

Iron deficiency is known to affect immune status by reducing the delayed-type hypersensitivity reaction, cytotoxic activity of phagocytes. A low plasma iron concentration also selectively inhibits proliferation of TH1 and not TH2 cells; thus, iron may be important for maintaining maternal health and reducing the risk of infection (22).

Low plasma zinc concentrations during pregnancy, resulting from low dietary bioavailability or very high amounts of copper in the diet that compete with zinc at absorption sites, have been associated with congenital abnormalities, abortions, intrauterine growth retardation, premature birth, and preeclampsia (23).

Few studies have been reported which correlates well with present study are as follows:

Trace elements deficiency (Zn, Cu & Fe) is associated with anemia and adverse effects on fetus and mother during pregnancy. Documented inverse correlation between copper and hemoglobin, especially among anemic pregnant women by Ma AG, et. al (24). Hemoglobin levels significantly correlated positively with zinc by Abdel Rahim et. al (25). Elemental interactions among trace elements such as copper, zinc, iron and magnesium has also been suggested to contribute to variations in the plasma levels of these trace elements and contribute to anemia by Bushra et. al (26). Zinc status account for hematological abnormalities in pregnant women by Kanagal DV et. al (23).

It appears to be a complex interrelation between iron, copper and zinc in absorption and utilization. In view of this the judicious supplementation of trace elements during pregnancy, is essential to maintain their optimum blood levels required for proper growth of fetus.

7. CONCLUSION:

From this study it can be concluded that trace elements investigation (Serum Copper, Serum Zinc and Serum Iron) will be a useful diagnostic test that can be performed to rule out micronutrient deficiencies in anaemic pregnant women. It may be due to a combination of trace element deficiencies and their interactions with each other. Deficiencies can exist because of losses or malabsorption associated with disease or inadequate intakes, lack of knowledge about adequate prenatal nutrition, or dietary taboos associated with pregnancy and lead to anaemia. Under these circumstances early nutritional anaemia biomarker such as Zinc, Copper and iron can be used which would help in the decision-making power by increasing diagnostic efficacy of anaemia and early treatment can be initiated to prevent abnormalities and mortality for mother and foetus both.

Conflict of Interest: The authors do not have any conflict of interest**.**
Source of Funding: Parul Institute of Medical Sciences & Research, Parul University.

Acknowledgement:

The authors would like to acknowledge & thank Dr.Geetika Madan Patel- Member, Governing body and Medical Director, Parul Sevashram, Hospital, Parul University for support and providing facilities to carry out this research work**.**

REFERENCES:

1. Oladapo AL, (2000): Nutrition in pregnancy: mineral and vitamin supplements: Am J Clin Nutr, 72, 280.
2. Hayes, Meghan, Larson & Lucia, (2012). Chapter 220: Overview of Physiologic Changes of Pregnancy, Principles and Practice of Hospital Medicine ,(The McGraw-Hill Companies, ISBN 978-0071603898).
3. Spencer BH, Vanderlelie JJ & Perkins AV, (2015): Essentiality of Trace Element Micronutrition in Human Pregnancy: A Systematic Review: J Preg Child Health, 2, 157.
4. J.B. Sharma & Meenakshi Shankar, (2010): Anemia in Pregnancy: *JIMSA,* 23, 4.
5. Government of India; Ministry of Health and Family Welfare; National Family Health Survey – 4: 2015 -16.
6. Pathak P, Kapil U, (2004): Role of trace elements zinc, copper and magnesium during pregnancy and its outcome: Indian J Pediar,71, 1003.
7. WHO. Micronutrient deficiencies. Iron deficiency anaemia, (2011) www.who.int/nutrition/topics/ida/en/index.html.
8. James PW, Tamerlan R, Nicolai P, Bradley AW, Nafisa BS, Rashed M, Vilma QT & Fabian R, (2018): Micronutrient Deficiencies, Over-and Undernutrition, and Their Contribution to Anemia in Azerbaijani Preschool Children and Non-Pregnant Women of Reproductive Age: Nutrients, 10, 1483.
9. Hurrell R & EgliI, (2010): Iron bioavailability and dietary reference values: Am J Clin Nutr, 91, (5) 1461S.
10. Prynne CJ, McCarron A, Wadsworth ME& Stephen AM, (2010): Dietary fibre and phytate— a balancing act: results from three time points in a British birth cohort: Br J Nutr,103, 274.
11. Tayrab, Amjad H, Hassan MI & Gaafar M, (2013): Serum Copper and Iron Status in Pregnant Women with Iron Deficiency Anemia: J Physiobiochem Metab, 2, 2.
12. Johnson-Wimbley TD & Graham DY, (2011): Diagnosis and management of iron deficiency anemia in the 21st century: Therapeutic Advances in Gastroenterology, 4177.
13. Iwona L, Rafał K, Mariusz G, Zuzanna G, Przemysław O & Joanna S, (2017): Selected trace elements concentrations in pregnancy and their possible role — literature review: Ginekologia Polska, 88, 509.
14. Naithani M, Bharadwaj J & Garg A, (2016): Study of relation between serum iron and copper levels in pregnant females of Uttarakhand, India: Acta Medica Inter, 3, 83.
15. Samira K, Hamed F & AbdolhaKim G, (2017): Minerals in Pregnancy and Lactation: A Review Article: J Clin Diagn Res, 11QE01.
16. Noura A, Hajera T, Huda A, & et. al, (2014): Analysis of serum trace elements-copper, manganese and zinc in preeclamptic pregnant women by inductively coupled plasma optical emission spectrometry: a prospective case-controlled study in Riyadh, Saudi Arabia: Int J Clin Exp Pathol,71, 900.
17. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, (2011). (WHO/NMH/NHD/MNM/11.1)
18. Ankita Abe & Yiamashit S, (1989): Clin. Chem., 35, 552.
19. Tetsuo Makino, (1991): Clin. Chem. Acta., 197, 209.
20. Callahan JH, Cook KO & Garcic A, (1979): Clin. Chem. Acta., 94, 115.
21. Salih E & Mahmood B, (2016): Quantitative study of some trace elements and blood parameters in the third trimester of Iraqi pregnant women with Pre-eclampsia: Iraqi J Science, 57, 2197.
22. Yoshida SH, Keen CL, Ansari AA, Gershwin ME, (1999): *Nutrition and the immune system*. (In: Shils ME, Olsom JA, Shike M, Ross AC, eds. Modern nutrition in health and disease. 9th ed. Baltimore: Williams and Williams), 725.
23. Kanagal DV, Rajesh A, Rao K, Shetty H, Shetty PK & Ullal H., (2014): Zinc and copper levels in preeclampsia: a study from coastal South India: Int J Reprod Contracept ObstetGynecol, 3, 370.
24. Ma AG, Chen XC, Xu RX, Zheng MC, Wang Y&Li JS, (2004): Comparison of serum levels of iron, zinc and copper in anaemic and non-anaemic pregnant women in China: Asia Pacific J Clin Nutr, 13, 348.
25. Abdelrahim II, Mahgoub HM, Mohamed AA, Ali NI, Elbashir MI & AdamI, (2009): Anaemia, folate, zinc and copper deficiencies among adolescent schoolgirls in Eastern Sudan. *Biol Trace Elem Res,*132, 60.
26. Bushra M, Elhssan EM, Ali NI, Osman E, Bakheit KH & Adam II, (2010) : Anaemia- zinc and copper deficiencies among pregnant women in Central Sudan. *Biol Trace Elem Res.,* 137, 255.