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Serum micronutrient levels, nucleic acid metabolism and antioxidant defences in pregnant Nigerians: implications for fetal and maternal health.

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Summary

Micronutrients regulate numerous metabolic processes in pregnancy but their possible antioxidant function and contributions of alterations in their metabolism to fetal and maternal morbidity and mortality have received insufficients attention. Serum levels of copper, manganese and zinc were determined in 40 pregnant Nigerian women spread across the three trimesters of pregnancy and compared with those of 25 non-pregnant women of similar demographic and anthropometric characteristics. Serum levels of uric acid were also determined in both groups of women. The mean serum levels of manganese and zinc were significantly lower in the pregnant than in the non-pregnant state ($P<0.02$, $P<0.002$), respectively. Unlike manganese and zinc, copper was singificantly elevated in the pregnant than in the non-pregnant state. The endogenous anti-oxidant, uric acid, was also significantly reduced in the pregnant than in the non-pregnant state ($P<0.001$). Copper levels increased progressively in all the three trimesters of pregnancy compared with controls ($P<0.001$). However, zinc levels declined steadily in all the 3 trimesters, but only the level of the third trimester was significantly different from the non-pregnant state ($P<0.05$). Unlike zinc, uric acid rose consistently in all the 3 trimesters compared with the non-pregnant state. Manganese and uric acid were significantly more elevated in the third than the first trimester. One way analysis of variance (ANOVA) and multiple comparisons (Tukey HSD) show that the differences in the antioxidant levels can be ascribed mainly to the second and third trimesters. The prevalence of zinc deficiency was 4.0% in the non pregnant state as compared to 22.5% in the pregnant subjects. The implications of micronutrient deficiencies and associated antioxidant status in pregnancy are discussed. Considering their role in pregnancy, prevention of such deficiencies and attendant oxidative stress may contribute to a reduction in the incidence of fetal and maternal ill-health, and complications of pregnancy. Interventions should be aimed mainly at the second and third trimesters.

Keywords: *Maternal health micronutrients, pregnancy, antioxidants, nucleic acids, cellular metabolism, oxidative stress, fetal well being.*

Résumé

Les micromolecules régularisent plusieurs processus métaboliques pendant la grossesse. Mais leur function d'antioxidant et leur contribution d'alterner le metabolisme aux fétus conduisent a la souffrance et à la mortalité maternelle ne recevant pas assez d'attention. Les taux de cuivre, de manganese , de zinc dans le serum ont été determinés chez 40 femmes nigériannes encientes durant les 3 trimestres de grossesse et comprarés à ceux de 25 femmes non-enceintes dans les memes conditions démographiques et anthropométriques. Les taux d'acide urique du serum étaient également determinés chez ces 2 groupes . Les taux moyen de manganése et du zinc dans le serum étaient significativement bas chez les femmes enceintes que chez celles pas enceintes ($P<0.002$; $P<0.002$) respectivement.. Le Cuivre comparé au maganes et au zinc était significativement élevé chez les femmes enceintes que chez celles pas enceintes. L'antioxidant endogéne, l'acide urique était aussi signficativement réduit chez les femmes enceintes que celles pas enceintes ($P<0.001$). Les taux du cuivre augmentait progressivement dans tous les 3 trimestres de grossesse comparé aux groupes de contrôle ($P<0.005$). Cependant, les taux du zinc réduiaient graduellement durant les 3 trimestres de grossesse ; mais seule ce taux du zinc au 3 trimestres était significativement different avec celle des femmes pas enceintes. Pas comme le zinc l'acide urique s'élevait gradement durant les 3 trimestres comparés à celles pas enceintes. Le manganese et l'acide urique étaient significativement plus elevés dans le 3 ieme trimestre qu'au 1ieme trimestre de grossesse. L'analyse de la variance (ANOVA) et des comparaisons multiples(Turkey HSD) montraient que, des differnces des taux d'antioxidant peuvent etre souscrite au 2 nd et 3 ieme trimestre de grossesse. Le taux deficitaire du zinc etait de 4.08% chez ceux non enceintes compares a 22.5% chez les sujects enceinte. Les implications des déficies des micromolecules et le status d'antioxidant associés durant la grossesse était discute. Considerant le role durant la grossesse, La prevention de tels déficies etl' action des antioxidants peuvent contribuer a la réduction de l'incidence de la santé médiocre des fétus et leurs meres et les complications de l'accouchement.L'intervention doit etre orienté a la 2ieme et 3ieme trimestre de la grossesse.

Introduction

Pregnancy is associated with a series of small, continous physiologic adjustments that affect the metabolism of all nutrients. About forty days after conception, the placenta, a complex organ of internal secretions, releases numerous hormones and enzymes into the maternal circulation which affect the metabolism of all nutrients. These adjustments in nutrient metabolism in addition to changes in the anatomy and physiology of the mother support fetal growth and development while maintaining maternal homeostasis and preparing for lactation [1] These processes account for the raised metabolic rate (hypermetabolic state) in the pregnant state. Oxidative damage is an inevitable side effect of cellular metabolism leading to genome instabilities (including telomere shortening mitochondrial mutation and chromosomal pathologies) as well as systemic aging [2]

The mother's nutrition from the moment of conception is an important factor in the development of the infants pathways and future wellbeing. As a component of prenatal care, micronutrient supplementation might reduce maternal morbidity and mortality directly by treating a pregnancy related illness or indirectly by lowering the risk of complication at delivery [3]. Accumulating data also suggest that micronutrient requirements depend on genetic characteristics and nutritional status of the Woman at conception [1]. Zinc defi-

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ciency for instance has been associated with congenital abnormalties, abortions, intrauterine growth retardation premature birth (4) pre-eclampsia and oxidative stress [5,6,7]. Inadequate zinc may predispose to hypertension in pregnancy and serum zinc concentrations have been found to show an inverse relationship to blood pressure [8]. Zinc deficiency can also affect immune response because it results in reduction of T cell development, thymic hormone release, T cell function and antibody synthesis [9].

Very importantly zinc plays an important role in nucleic acid metabolism and protein synthesis [10]. While the information on the role of Manganese in pregnancy is scanty [3] the importance of copper is more commonly related to its role in haemopoiesis [11]. Copper, Manganese, zinc and uric acid (end product of nucleic acid metabolism) all belong to the antioxidant defence system [12]. Requirement for most micronutrients increases during pregnancy because of fetal demands [3]. This is consistent with a hyper-metabolic state which will in turn be associated with increase free radical generation (endogenous sources) [12]. To protect fetal development, several mechanisms have evolved to ensure that fetal nutrients including dietary antioxidants are met. However, in developing countries where malnutrition, malabsorption associated with disease, dietary phytate and taboos associated with pregnancy prevail [13]. The situation is uncertain deficiency of micronutrients may have potential adverse consequences for both mother and child including wide- spread damage to a wide range of molecular species such as lipids, proteins and nucleic acids. Knowledge of micronutrients status in pregnancy in developing countries is necessary because of the widespread pregnancy related complications resulting in high fetal and maternal morbidity and mortality. Though there is a relatively large body of literature on studies on micronutrient in the reproductive life of Nigerian Women, Olatunbosun *et al* [14], Mbofung and Atinmo [15, 16], Ajose *et al* [17], all these studies appear to have focused on gestation, anthropometric factors, haemopoietic activity and correlations to explain changes in micronutrient level especially copper and zinc. The interrelation of micronutrient status, nucleic acid metabolism and antioxidant defences has received little attention. Yet in recent years, a substantial body of evidence has developed, supporting a key role for free radicals in many fundamental cellular reactions and suggesting that oxidative stress might be important in the pathophysiology of common diseases [12]. Some of these diseases take their root from fetal life [18]. Furthermore, previously emphasis has been on iron, folate or a combination of iron and folate and calcium intake [3].

Moreover, previous reports also indicate that the traditional micronutrients (iron, and folate) and the mineral calcium, alone cannot ensure desirable maternal health [19-21]. Additionally iron is a pro-oxidant which will increase the free radical burden [12] in pregnancy.

Uric acid is closely associated with pregnancy. It was previously popularly used as a biochemical marker of pre-eclampsion and its management. In recent years it has assumed a new role. Though it is not a micronutrient, it is related to the micronutrients (especially antioxidant micronutrients) because it is an endogenous antioxidant [22]. The aim of this study, therefore, was to determine the micronutrient status specifically copper, manganese and zinc and also uric level in pregnant Nigerians to examine their relationship and possible implications in the distressing fetal and maternal morbidity and mortality rates in Nigeria.

Subjects and methods

Subjects

Sixty-five subjects were selected for this study. They comprised of 40 pregnant women attending the Antenatal Booking Clinic of the University College Hospital (UCH), Ibadan, Nigeria, and twenty-five non-pregnant individuals as control. The latter were drawn from the population of female students and staff of the hospital. The women in both groups were in good general health and were not on a special diet or receiving any chronic drug therapy. Informed consent for participation was obtained from each participant and an approval for the study was also obtained from the Ethical Committee of the hospital. The design of the study was essentially cross sectional.

Clinical data and anthropometric measurements

Information on maternal age, height, weight, and parity was obtained at the first prenatal visit. Gestational age (in weeks) at the first visit was estimated based on the first day of the last menstrual period (LMP). The pregnant women were made up of 5 primigravidae and 35 multigravidae in the three trimesters of pregnancy. Ten women were in the first trimester and 15 each in the second and third trimesters of pregnancy.

Specimen Collection

Ten millilitres of venous, non-fasting (late morning; 11.00 a.m. – 12.00 noon) blood was collected from each subject and dispensed into two specimen containers - 2.0 mls were dispensed into EDTA containers for packed cell volume (PCV) determination while 8.0 mls were dispensed into trace element-free and anticoagulant free tubes (Vacutainer, Becton Dickinson, Rutherford, NJ) to obtain serum for biochemical assays. The sera were kept frozen at – 20°C until the time for analysis. Urinalysis was also performed on all patients and controls by means of N-Multistix SG urinalysis strips (Ames, Elkhart Indiana, USA)

Analytical Methods

Packed Cell Volume was determined by standard haematological procedures. Copper (Cu) was determined by the methods of Osheim [23] using flame atomic absorption spectrophotometry (FAAS). Manganese (Mn) was determined also by FAAS using the method of Neve and Leclercq [24] while Zinc was determined by the selected method of Smith *et al* [25], also employing FAAS. Uric acid was determined by the method described by Fassati *et al*. [26]. Meticulous attention and strict adherence to standard procedures of trace element analysis including recovery studies were adopted to ensure quality control. Additionally, all materials used in specimen collection, processing and analysis were evaluated for contamination with zinc and copper by rinsing vessels with ultra pure water and assaying for the elements. These yielded no significant concentrations of these (i.e. negligible).

Statistical Analysis

Basic statistical analysis were performed using student's t-test of unpaired data. It was also used to compare values between the pregnant and non-pregnant states and among the three trimesters of pregnancy. Followed by stepwise analysis to compare micronutrient levels and the product of nucleic acid metabolism, uric acid in the three trimesters. This was performed first with the t-test, followed by one way ANOVA and the multiple comparison test (Turkey HSD). All analysis were performed with SAS (Version 7 Ts Ti SAS Institute Inc. Cary,

NC). All results were considered statistically significant at ($P < 0.05$). All results were reported as mean ± SEM.

Results

The mean age and anthropometric indices are all shown in Table I. The mean age (29 ± 1.5 years) and height (1.60 ± 0.7 metres) of the pregnant women were quite similar to those of the women in the control group, i. e. 25 ± 1.1 years and 1.59 ± 0.01 metres, respectively. Table 2 shows the distribution of the pregnant women in the three trimesters of pregnancy by parity and packed cell volume. The mean of the PCV for the non-pregnant group was 37. 3 ± 0.6 %.

Table 1: Anthropometric Indices of Pregnant Subjects by Trimester of Pregnancy.

Indices	Trimester of Pregnancy		
	First (n = 10)	Second (n = 15)	Third (n = 15)
Age (years)	28.4 ± 1.8	29.2 ± 1.4	30.1 ± 1.3
Weight (kg)	57.7 ± 0.6	64.3 ± 1.0	67.7 ± 1.3
Height (m)	1.61 ± 0.2	1.60 ± 0.2	1.60 ± 0.3
Body Mass Index (kg/m^2)	22.4 ± 0.2	25.0 ± 0.5	26.3 ± 0.4

For the non-pregnant subjects: Mean Age =25.0 ± 1.1; Mean Height = 1.59 ± 0.01.

Table 2: Distribution of Subjects by Parity and Packed Cell Volume.

Indices	Trimester of Pregnancy		
	First (n = 10)	Second (n = 15)	Third (n = 15)
Parity	2.0 ± 0.1	2.0 ± 0.3	2.0 ± 0.5
PCV (%)	33.3 ± 1.1	34.1 ± 0.7	33.4 ± 0.8

For the non-pregnant women (n = 25): mean packed cell volume (PCV) was 37. 3 ± 0.6%

The serum levels of the three micronutrients analysed and uric acid are depicted in Table 3. Copper was significantly elevated in the pregnant than in the non-pregnant state. However, manganese and zinc were significantly lower in the pregnant than in the non-pregnant state. Uric acid, an endogenous antioxidant was also significantly reduced in the pregnant than in the non-pregnant state.

Table 3: Comparison of Serum Levels of Micronutrients (Cu, Mn, Zn) and Uric Acid in pregnant and non-pregnant women

Micronutrient	Pregnant Subjects (n = 40)	Non-pregnant Subjects (n = 25)	t	p value
Copper (ug/dl)	204.7 ± 5.3	137.4 ± 5.8*	8.3	<0.001
Manganese (ng/ml)	8.7 ± 0.4	10.4 ± 0.7*	2.4	< 0.02
Zinc (ug/dl)	87.3 ± 2.7	97.4 ± 2.6*	2.5	< 0.02
Uric Acid (mg/dl)	2.8 ± 0.1	4.9 ± 0.2*	10.5	< 0.001

* *Statistically significant (p value < 0.05)*

A comparison of the levels of the micronutrients in the three trimesters of pregnancy with the non-pregnant state shows progressively increasing significant levels of copper in the three trimesters of pregnancy (Table 4). The mean serum

Table 4: Comparison of Serum Levels (mean ± SEM) of Micronutrients and Uric Acid in pregnant and non-pregnant women.

Micronutrient	Non-pregnant Women	Trimester of Pregnancy		
	(n = 25)	First (n = 10)	Second (n = 15)	Third (n = 15)
Copper (ug/dl)	137.4 ± 5.8	185.6 ± 10.8*	200.4 ± 7.8*	220.4 ±7.9
Manganese (ng/ml)	10.4 ± 0.7	7.4 ± 0.9*	8.4 ± 0.5	9.9 ± 0.5
Zinc ug/dl)	97.4 ± 2.6	95.2 ± 4.5	92.1 ± 4.4	83.3 ± 4.5
Uric Acid (mg/dl)	4.9 ± 0.2	1.9 ± 0.2*	2.0 ± 0.1*	3.0 ± 0.2

* *Statistically significant (p value < 0.05)*

Table 5: Comparison of Serum Levels of Micronutrients (Cu, Mn, Zn) and Uric Acid at different trimesters of pregnancy.

A. Between 1st and 2nd Trismester

Micronutrient	First Trimester (n = 10)	Second Trimester (n = 15)	t	P value
Copper (ug/dl)	185.6 ± 10.8	200.4 ± 7.8	1.2	> 0.05
Manganese (ng/ml)	7.4 ± 0.9	8.4 ± 0.5	1.1	> 0.05
Zinc (ug/dl)	95.2 ± 4.5	92.1 ± 4.4	0.5	> 0.05
Uric Acid (mg/dl)	1.9 ± 0.2	2.0 ± 0.1	0.5	> 0.05

(B) Between 1st and 3rd Trimesters

Micronutrient	First Trimester (n = 10)	Third Trimester (n = 15)	t	p value
Copper (ug/dl)	185.6 ± 10.8	220.4 + 7.9*	2.7	< 0.02
Manganese (ng/ml)	7.4 ± 0.9	9.9 + 0.5*	2.7	< 0.02
Zinc (ug/dl)	95.2 ± 4.5	83.3 + 4.5	1.7	> 0.05
Uric Acid (mg/dl)	1.9 ± 0.2	3.0 + 0.2*	0.5	< 0.01

(C) Between 2nd and 3rd Trimesters

Micronutrient	Second Trimester (n = 15)	Third Trimester (n = 15)	t	p value
Copper (ug/dl)	200.4 + 7.8	220.4 + 7.9	1.8	> 0.05
Manganese (ng/ml)	8.4 + 0.5	9.9 + 0.5*	2.1	< 0.05
Zinc (ug/dl)	92.1 + 4.5	83.3 + 4.5	1.3	> 0.05
Uric Acid (mg/dl)	2.0 + 0.1	3.0 + 0.2*	4.3	< 0.001

All values are mean (+ SEM)
* *Statistically significant (p value < 0.05)*

levels of manganese, although lower than the non-pregnant state, rose steadily from the first to the third trimester. Zinc also showed a steady decline in value from the first to the third

trimester. However, only the level in the third trimester was significantly different from that of the pre-pregnant state (P <0.05). Uric acid exhibited a significant decrease in all three trimesters compared with the non-pregnant state.

Table 5 shows a comparison of the mean serum levels of the micronutrients and urate across the three trimesters of pregnancy. A comparison of the mean levels of the micronutrient and uric acid between the first and second trimesters revealed no significant difference in all respects. In contrast, a comparison of mean values in the first and third trimesters showed that copper and manganese were significantly more elevated in the third trimester than in the first trimester (P <0.02). The mean level of zinc was however, lower in the third than in the first trimester but this difference did not reach statistical significance. Uric acid levels however, were significantly higher in the third than in the first trimester (P <0.01).

A comparison of the second and third trimesters showed no significant difference in copper levels. Manganese however, was significantly more elevated in the third trimester than in the second trimester (P <0.05) . Again, uric acid was significantly more elevated in the third trimester than in the second trimester (P <0.001). A-one way analysis of variance (ANOVA) based on the three trimesters of pregnancy, serum micronutrient levels and the product of nucleic acid metabolism show that Copper, Manganese and uric acid were significantly different as already indicated by the t-test ($F = 3.96$, $P < 0.028$; $F = 3.949$, $P < 0.028$ and $F = 6.814$ $P < 0.000$ respectively.

The multiple comparisons (Tukey HSD) show that the differences arose mainly between the second and third trimesters for the micronutrients copper, manganese and the product of nucleic acid metabolism uric acid ($P < 0.024$, $P < 0.028$ and $P < 0.000$ respectively). Zinc as with the t-test did not show any variation among the 3 trimesters either with ANOVA or the multiple comparison tests.

Table 6: Prevalence of Zinc Deficiency in the non-pregnant and pregnant women.

Status of Subjects	Women with low levels of Zinc*	
	Number	Percentage
Non-pregnant women (n = 25)	1	4.0
First Trimester (n = 10)	1	10.0
Second Trimester (n = 15)	3	20.0
Third trimester (n = 15)	5	33.3
All pregnant women (n = 40)	9	22.5

**A low level is defined as that below the lower limit of reference range.*

The prevalence of zinc deficiency (levels below the lower limit of normal, i.e 76 ug/dl) was 4% in the non-pregnant state and 22.5% in the total population of pregnant subjects (Table 6). There was a progressive increase in the prevalence of deficiency from the first to the third trimester. The prevalence was 10% in the first trimester, 20% in the second trimester and 33% in the last trimester.

Discussion

The possible contributions of alterations in micronutrient metabolism to maternal morbidity and mortality has been speculated [10]. The importance of micronutrients is revealed by the diversity of metabolic processes they regulate. During pregnancy there is increased metabolic and synthetic activities which are catalysed by enzymes and co-enzymes. Moreover, oxidative damage is an inevitable side effect of cellular metabolism which is enhanced in the pregnant state leading to genome instabilities (including telomere shortening, mitochondria mutation and chromosomal pathologies) [2]. These require micronutrients as co-factors. Unlike iron, a pro-oxidant which may lead to increase in free radical load, and folate that are commonly prescribed and clinically evaluated during pregnancy, microminerals such as zinc, manganese and copper are often ignored. Yet, these are biochemically very important and may regulate the status and bioavailability of the micronutrients, especially the vitamins and important members of the antioxidant defence system.

The finding of significantly reduced zinc levels in the pregnant state is consistent with earlier reports [27-30]. Expansion in plasma volume associated with the pregnant state is often given as an explanation for the decline of serum levels of most biochemical analytes. This can only be partly correct as the concentrations of some nutrients decline while others either remain unchanged or may increase [3]. Some other explanations therefore appear plausible. An important reason for a reduced zinc level is an increased demand. Zinc is mainly an intracellular cation required to serve either a catalytic or structural role in over 200 enzymes in mammals. Zinc dependent enzymes participate in many components of macronutrient metabolism and cell replication involving nucleic acid which are pronounced in pregnancy owing to the increased metabolic rate and tissue synthesis. It has been reported that free radical load is increased in pregnancy [31] and is associated with increased oxidative stress. Another zinc containing enzyme, super oxide dismutase, protects against free radical damage [32]. Also, relatively more oestriols are produced in pregnancy leading to an increased formation of free radicals which are capable of mediating tissue damage both in the mother and the growing foetus [33].

Inadequate intake of zinc may be another explanation for the significantly reduced zinc levels in pregnant Nigerians. Indeed, a study in a similar socio-economic environment indicated that zinc levels [34] were significantly reduced in pregnancy. The result from this study shows that 10% of women in the first trimester, 20.0% of the women in the second trimester and 33% of those in the third trimester of pregnancy exhibited zinc levels below the lower limit of the reference range. These data suggest a need for the supplementation of this micronutrient in pregnancy. Indeed, an optimum level of zinc is desirable in pregnancy considering its involvement in a wide range of metabolic, antioxidant and synthetic activities.

Reduction in zinc levels in pregnancy is of considerable concern because of the significant role it plays in the metabolism of other micronutrients which are important for maternal and fetal health. Vitamin A metabolism and bioavailability is dependent on zinc status [35]. The deficiency of this vitamin which has been shown to increase the risk of maternal mortality is associated with premature birth, intra-uterine growth retardation, low birth-weight [36, 37] and antepartum haemorrhage due to abruptio placenta [38]. Additionally, zinc appears to modulate the status of the very powerful antioxidant Vitamin E [39].

Information on the role of manganese in pregnancy is scanty [3]. It is however, known to be required for prothrombin synthesis [40]. This may be a very important factor in post-partum haemorrhage, a condition that is associated

with a high mortality rate in this environment. The observed increase in manganese level from the first to the third trimester may be required for two reasons. It may be the need to conserve the micronutrient for an increased prothrombin sythesis in the later stages of pregnancy in order to forestall excessive bleeding at delivery. Secondly, manganese is an antioxidant (MnSOD) and a component of mitochondria. Thus, it could be an endogenous antioxidant response to ameliorate the oxidative stress which follows an increased steroid production and its attendant free radical load in pregnancy. This probably ameliorates the damage caused by free radicals. Therefore, inadequate manganese may contribute to oxidative stress.

The significantly elevated copper levels in the pregnant state is again consistent with previous reports [41]. The highest level was recorded in the third trimester of pregnancy. This observed increase has traditionally been primarily attributed to oestrogen stimulated ceruloplasmin synthesis. Mbofung and Atinmo [16] reported that this may be diet dependent and ratio of copper: zinc. Ceruloplasmin plays dual roles; it is an acute phase reactant reflecting the stress of pregnancy. It is also an endogenous antioxidant (Cu-Zn SOD) [42] which ameliorates the oxidative stress arising from increasing free radical load. Copper exists in the blood as ceruloplasmin, a specific copper transporting protein with the ability to oxidize ferrous to ferric iron. In copper deficiency, iron is excreted in the urine in the ferrous state instead of being conserved in combination with transferrin, which only binds ferric iron resulting in secondary iron deficiency. This form of iron deficiency is often refractory to iron supplementation.

The significantly decreased uric acid level in the pregnant state is again consistent with the free radical antioxidant hypothesis in the pregnant state. An excessively elevated uric acid level used to be one of the triads for the diagnosis of pre-eclampsia. It is likely that decreased urate level in-fact reflects oxidative stress – a state of imbalance between the rate of production of free radicals and antioxidant concentrations. Uric acid is now considered an endogenous antioxidant [22]. The decrease may reflect excessive consumption in the phase of significantly decreased components of the antioxidant defence system. Thus, the observed decrease in uric acid and increase in manganese and copper may, all put together, suggest a dose response relationship to the free radical load in pregnancy. The change in the opposite direction of uric acid compared to others in addition to excessive consumption, could be because it is endogenous [22] while others are either dietary or have dietary components. It is likely that when this response is not elicited, there are added risks to maternal morbidity and mortality. Oxidative stress resulting from dysequilibrium between reactive oxygen species (ROS) and antioxidant defences is associated with damage to a wide range of molecular species including lipids, proteins and nucleic acids, thus enhancing susceptibility to disease.

An adequate evaluation of micronutrient status may help in assessing the risk of maternal morbidity and mortality, probably in part attributed to oxidative stress. This has tended to be restricted to iron and folate in the past [43]. The practice should be extended to other micronutrients such as copper, manganese, and especially zinc which is so central in the metabolism and bioavailability of other micronutrients such as Vitamins A and E (also antioxidants) as well as nucleic acid metabolism that are very essential for maternal and fetal health. Optimal micronutrient status (thus adequate antioxidant status) may contibute significantly to a reduction in the incidence of ill health and some life-threating complications of pregnancy that are still common in many developing countries. Indeed, giving a priority to antioxidant micronutrient status in pregnant Nigerians may be an additional weapon against the distressing maternal morbidity and mortality rates in the country.

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