Maternal Serum Concentrations of Micronutrients and Risk of Preterm Birth: A Case-Control Study

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Abstract: ***Background**: Micronutrients are essential inorganic constituents for human health although only needed in minute quantities. Suboptimal status of micronutrients, whether deficiency or excess, could lead to detrimental pregnancy outcome. Deficiency or toxicity of those elements could lead to preterm labor. **Patient and Methods**: This is a case-control study that included 80 patients (40 cases and 40 controls) and was conducted in Baghdad Teaching Hospital/ Medical city, Baghdad in the period from the 1st of January 2023 to the 30th of August 2023. Preterm birth was defined as birth at gestational age less than 37 weeks and term pregnancy ≥ 37 completed weeks. Testing for blood Copper, Zinc, Manganese, Cobalt, and iron levels were conducted in the Iraqi Poisoning Consultation Center of Baghdad Medical City. **Results**: The mean age of women with term labor was 28.7 ± 6.2 and among women with term labor was 27.3 ± 6.5 with no significant difference in mean of age between both groups (p=0.35). measurement of Hb among preterm group was 11.8 ± 1.4 while it was 12.9 ± 0.8 among term group with significant lower mean of Hb among preterm group (p=0.001). For BMI, it was 24 ± 3 among term group and 22.6 ± 2 among preterm group with no significant difference between both groups (p=0.056). The mean Copper level among term group (131.7 ± 16.7) was significantly lower than among preterm group (138.8 ± 10.6) (p=0.002). The mean of zinc level among preterm group (71.3 ± 11.4) was significantly lower than mean of term group (90.1 ± 21.4) (p=0.001). The mean manganese level among preterm group was 0.011 and among term group was 0.014 with no significant difference between both group (p=0.071). By studying the cobalt level, the mean of cobalt level among preterm cases (0.088 ± 0.02) was significant lower in compare to mean among term cases (0.099 ± 0.01) (p=0.029). The mean iron level among preterm cases (94.5 ± 20.6) was significantly lower in comparison to mean among term group (147.9 ± 18.8) (p=0.0001). **Conclusion**: Maternal blood Cobalt, Zinc, and Iron levels were significantly low among women with preterm birth in comparison to women with term birth. Copper level was significantly higher among women with preterm birth in comparison to women with term birth. However, majority of cases were fall with in normal range of Copper level.*

Keywords: Micronutrients, Pregnancy, Preterm Mothers

1. Introduction

Preterm birth remains the leading cause of mortality and morbidity of children under the age of 5 in global scale, particularly in a developing country such as Indonesia. As much as 15 out of 100 babies are delivered prematurely, contributing to 35.5% of neonatal death in the country.[1]

The cellular apoptosis that transmits an inflammatory signal, senescent placental cells, and its changes in placental membrane were hypothesized to stimulate parturition, both term and preterm birth, called as “common pathway.” The premature aging of the placenta caused by oxidative stress is believed to stimulate the common pathway prematurely. Reactive Oxygen Stress (ROS), the source of oxidative stress, activates NF-kappa B which further stimulates COX-2 and proinflammatory cytokines. Infection and exogenous factor such as lead exposure also upregulate ROS, increasing the risk of preterm birth. Micronutrients such as trace elements and vitamins such as copper, zinc, manganese, selenium, and vitamin A serve as endogenous antioxidant that counterbalances the oxidative stress, as well as regulating inflammatory response.[2]

Concentrations of micronutrients is affected by dietary habit, lifestyle, and environmental condition. Following industrial revolution, mercury (Hg) and lead (Pb) are gaining attention regarding environmental exposure and their effects in the body. During pregnancy, even low lead concentration could have adverse effects such as developmental delays, low birthweight, and miscarriage.[3]

Micronutrient deficiencies are common among women of reproductive age (15 to 49 years of age), especially those residing in low- and middle-income countries where diets often lack diversity and fortified foods are less available.

Infections and chronic illness can also contribute to micronutrient deficiencies by directly inhibiting nutrient absorption. Micronutrient deficiencies are exacerbated during pregnancy due to increased requirements of the growing fetus, placenta and maternal tissues. An inability to fulfil the increased demands results in potentially adverse effects on the mother and the fetus. Additionally, there can be sustained intergenerational effects. Maternal malnutrition has been shown to affect both short-term and long-term outcomes for the offspring, including growth, neurodevelopment and cognition, and cardiometabolic, pulmonary, and immune function.[4]

Pregnancy represents a period of major physiological and metabolic change, in order to ensure proper fetal growth and development, as well as maternal preservation and survival.1 Adequate pregestational nutritional status, as well as proper gestational weight gain and dietary intakes are mandatory to promote these processes and to avoid potentially adverse maternal and pregnancy outcomes.[2]

Therefore, it is important to evaluate, monitor, and if appropriate, make changes to improve maternal nutritional status both before and during pregnancy.[5]

Micronutrient intake is known to affect all stages of female reproductive period. Starting as early as the periconceptional period, embryonic morphological development has been definitely associated with maternal folic acid intake and one-carbon metabolism, leading to the strong recommendation of the WHO to supplement all women of childbearing potential with folic acid 400 µg daily. Furthermore, reproductive performance and consequent impaired fertility have been associated with nutrition, with adherence to healthy dietary patterns and intake of folic acid and omega-3 fatty acids found to be related to better fertility and higher live birth rates in artificial reproductive procedures.[6]

Nutrition has been additionally associated with fetal growth, preterm delivery and maternal hypertensive disorders through the modulation of placental function and inflammatory pathways. Finally, maternal nutrition in the postpartum period has been related to neonatal growth and maternal health and lactation.[7]

Patients and Methods

The study has been conducted in Baghdad Teaching Hospital/ Medical city, Baghdad. The data was collected from the 1st of January 2023 to the 30th of August 2023.

An official letter of approval has been obtained from the scientific committee of the scientific council of Obstetrics and Gynecology/Iraqi Board for Health Specializations.

An analytic case control design has been chosen for this study.

A total number of 80 pregnant women in labor from Baghdad were included in the present study:

- Case group: include 40 women with spontaneous preterm labor.
- Control group: include 40 women, term, in labor.

The Gestational age was calculated depending on the mother's LMP and first trimester ultrasound scan. Preterm birth was defined as birth at gestational age less than 37 weeks and term pregnancy ≥ 37 completed weeks.

Full history and thorough general and obstetrical examination were done for all pregnant women. Basic sociodemographic and obstetric data were collected (age, parity, gestational age, past medical history, pre-pregnancy BMI, birth weight, and husband's occupation).

An amount of 10 cc of blood was collected from pregnant women for general investigations: (CBC, RBS, RFT, LVT, TFT, Blood group and RH) and for test for blood copper, zinc, Manganese, cobalt, and iron levels.

Testing for blood copper, zinc, Manganese, cobalt, and iron levels was conducted in the Iraqi poisoning consultation center (P.C.C) in Medical City/Baghdad. Blood samples were put in shaker for 1 hour, after which 2.5 ml of trichloroacetic acid was added to 2.5 ml of blood. The mixture was applied in a centrifuge rotating in a speed of 3000 rounds/minute for a total of 10 minutes.

The normal range for maternal blood , minerals was as follow:

1) Copper concentration: 80 – 150 Mg/dl
2) Zinc concentration: 80 – 150 Mg/dl
3) Manganese concentration: 0.00 – 0.025 Mg/dl
4) Cobalt concentration: 0.07 – 0.15 Mg/dl
5) Iron concentration: 60 - 170 mcg/dl
6) Hb level was measured and the definition of anemia was as follow (WHO recommendation):
   - Sever: < 7g/dL
   - Moderate: 7 – 9.9 g/dL
   - Mild: 10 -10.9 g/dL

Mothers with the following conditions were excluded:

- Pregnancy-induced hypertension.
- Preeclampsia.
- Gestational DM.
- Heart disease.
- Thyroid related diseases.
- Twin pregnancy.
- Stillbirth.
- History of previous preterm labor.
- Alcoholism
- Who already received multivitamin supplement during pregnancy
- Smokers
- Unplanned stress.
- Still birth, congenital abnormalities.
- Uterine anomalies.
- Cervical surgery.
- Genital tract infection (e.g. bacterial vaginosis, UTI).
- Vaginal bleeding (previa).
- Polyhydramnios.
- BMI < 18 kg/m^2.

The collection of samples each week were collected from the participant.

The processing of sample and measurement of trace elements was conducted in Poisoning Concultation Center (P.C.C), Baghdad, Iraq.

Verbal consent has been obtained from all participants before data collection.

Data entry was done using Microsoft Excel 2019. Data was recorded into different quantitative and qualitative variables for the purpose of analysis.

Analysis was done using statistical package for social sciences (SPSS version 26).

Data was summarized using measures of frequency (mean), dispersion (standard deviation), tables and graphs. A two-tailed p value of less than or equal to 0.05 was assigned as a criterion for declaring statistical significance.

2. Results

There were 80 women included in this study divided for two groups based on gestational age of delivery. Group A, consist

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of 40 women who delivered their baby at Term, and Group B, also 40 women who delivered their baby at Preterm.

The mean age of women with term labor was 28.7 ± 6.2 and among women with term labor was 27.3 ± 6.5 with no significant difference in mean of age between both groups (p=0.35). Also, the age category distribution showed that majority of women, weather preterm or term groups, were between 20 – 35 years old with no significant difference in distribution (p=0.14). For the parity, more than 65% of included women among both groups were multigravida with no significant difference between both groups (p=0.81). regarding the address, almost half of participants were lived in urban, and for occupation, majority of participants were housewives, with no significant difference between both groups (p>0.05) (Table 1).

Table 1: Demographic Characteristics of studied groups

Variables		Preterm	Term	p-Value
Age (years)	< 20	6 (15%)	2 (5%)	0.17*
	20-35	25 (62%)	27 (67.5%)	
	≥ 35	9 (22.5%)	11 (27.5%)	
	Mean ± SD	27.3 ± 6.5	28.7 ± 6.2	0.35**
Parity	Primigravida	14 (35%)	13 (32.5%)	0.81*
	Multigravida	26 (65%)	27 (67.5%)	
Residence	Urban	27 (67.5%)	20 (50%)	0.11*
	Rural	13 (32.5%)	20 (50%)	
Occupation	Housewife	27 (67.5%)	32 (80%)	0.2*
	employee	13 (32.5%)	8 (20%)	

*: Chi-Square, **: independent sample t test.

The measurement of Hb among preterm group was 11.8 ± 1.4 while it was 12.9 ± 0.8 among term group with significant lower mean of Hb among preterm group (p=0.001). For BMI, it was 24 ± 3 among term group and 22.6 ± 2 among preterm group with no significant difference between both groups (p=0.056) (Table 2 & 3).

Table 2: Hemoglobin level of studied groups

Hb Level (g/dl)	Preterm	Term	p-Value
7 - 9.9	6 (15%)	1 (2.5%)	0.0001*
10 – 10.9	9 (22.5%)	0	
≥ 11	25 (62.5)	39 (97.5)	
Mean ± SD	11.8 ± 1.4	12.9 ± 0.86	0.001**

*: Chi-Square, **: independent sample t test.

Table 3: BMI level of studied groups

BMI (kg/m^2)	Preterm	Term	p-Value
< 19.5	0	1 (2.5%)	0.072*
19.5 - 25	34 (85%)	24 (60%)	
25- 30	5 (12.5%)	14 (35%)	
> 30	1 (2.5%)	1 (2.5%)	
Mean ± SD	22.6 ± 2.8	24 ± 3.3	0.56**

* : Chi-Square, **: independent sample t test.

The mean Copper level among term group (131.7 ± 16.7) was significantly lower than among preterm group (138.8 ± 10.6) (p=0.002). While based on normal value for copper per WHO, only 5 cases consider had high level of copper among preterm group and 4 cases among term group with no significant difference in distribution between both groups (p=0.12) (Table 4).

Table 4: Copper level of studied groups

Copper level	Preterm	Term	p-Value
Normal	35 (87.5%)	36 (90%)	0.12*
High	5 (12.5%)	4 (10%)	
Mean ± SD	138.8 ± 10.6	131.7 ± 16.7	0.002**

* : Chi-Square, **: independent sample t test.

The linear Regression analysis of the studied factors that associated with Cu showed that, Zinc, Mn, and Fe were associated with Co level (Table 5).

Table 5: Copper level correlation with studied factors

Model	Unstandardized Coefficients		p-Value	95.0% Confidence Interval for B	
	B	St. Error		Lower bound	Upper bound
Age	0.017	0.233	0.943	-0.448	0.481
Hb	0.686	1.15	0.553	-1.607	2.979
BMI	-0.155	0.479	0.748	-1.11	0.8
Zn	-0.433	0.129	0.001	-0.691	-0.176
Mn	2766.175	580.835	0.0001	1608.303	3924.048
Co	-186.68	99.108	0.064	-384.248	10.887
Fe	-0.119	0.05	0.021	-0.219	-0.018

The mean of zinc level among preterm group (71.3 ± 11.4) was significantly lower than mean of term group (90.1 ± 21.4) (p=0.001). Also, based on normal value for zinc per WHO, they were significant higher participants among preterm group with low level of zinc in compare to term group (p=0.02) (Table 6).

Table 6: Zinc level of studied groups.

Zinc Level	Preterm	Term	p-Value
Normal	7 (17.5%)	24 (60%)	0.02*
Low	33 (82.5%)	16 (40%)	
Mean ± SD	71.3 ± 11.4	90.1 ± 21.4	0.0001**

*: Chi-Square, **: independent sample t test

The linear Regression analysis of the studied factors that associated with Zinc showed that, Cu and Mn were associated with zinc level (Table 7).

Table 7: Zinc level correlation with studied factors

Model	Unstandardized Coefficients		p-Value	95.0% Confidence Interval for B	
	B	St. Error		Lower bound	Upper bound
Age	0.090	0.197	0.648	-0.303	0.488
Hb	1.297	0.965	0.183	-0.627	3.221
BMI	0.474	0.402	0.243	-0.328	1.276
Cu	-0.311	0.093	0.001	-0.496	-0.126
Mn	3058.933	434.195	0.000	2193.381	3924.485
Co	67.260	85.650	0.435	-103.48	238.001
Fe	0.003	0.044	0.953	-0.086	-0.091

The mean manganese level among preterm group was 0.011 and among term group was 0.014 with no significant difference between both group (p=0.071). Also, based on normal value for manganese per WHO, only 2 cases presented with high level of manganese among preterm group with no significant difference in distribution between both groups (p=0.54) (Table 8).

Table 8: Mangenes level of studied groups

Mangenes Level	Preterm	Term	p-Value
Normal	38 (95%)	40 (100%)	0.54*
High	2 (5%)	0	
Mean ± SD	0.011 ± 0.005	0.014 ± 0.003	0.071 **

*: Chi-Square, **: independent sample t test

The linear Regression analysis of the studied factors that associated with Mn showed that, Cu, Zn, Co and Fe were associated with Mn level (Table 9).

Table 9: Mn level correlation with studied factors.

Model	Unstandardized Coefficients		p-Value	95.0% Confidence Interval for B	
	B	St. Error		Lower bound	Upper bound
Age	-6.390E-5	0.0001	0.119	0	0.001
Hb	-7.394E-5	0.0001	0.718	0	0.001
BMI	-2.739E-5	0.0001	0.747	0	0.001
Cu	8.660E-5	0.0001	0.0001	0	0.001
Zn	0	0.0001	0.0001	0	0.001
Co	0.072	85.650	0.0001	0.041	0.104
Fe	2.326E-5	0.0001	0.010	0	0.001

By studying the cobalt level, the mean of cobalt level among preterm cases (0.088 ± 0.02) was significant lower in compare to mean among term cases (0.099 ± 0.01) (p=0.029). The level classification of cases based on normal value for cobalt per WHO showed that there were significant higher number of patients with lower level of cobalt among preterm (25%) in compare to term cases (2.5%) (p=0.003) (Table 10).

Table 10: Cobalt level of studied groups

Cobalt Level	Preterm	Term	p-Value
Normal	30 (75%)	39 (97.5%)	0.003*
Low	10 (25%)	1 (2.5%)	
Mean ± SD	0.088 ± 0.02	0.099 ± 0.01	0.029**

*: Chi-Square, **: independent sample t test.

The linear Regression analysis of the studied factors that associated with Co showed that only Mn was associated with Co level (Table 3.11).

Table 11: Copper level correlation with studied factors.

Model	Unstandardized Coefficients		p-Value	95.0% Confidence Interval for B	
	B	St. Error		Lower bound	Upper bound
Age	0	0.000	0.2	0	0.001
Hb	0	0.001	0.846	-0.003	0.002
BMI	0	0.001	0.598	-0.001	0.001
Cu	0	0.000	0.064	-0.001	0.00
Zn	0	0.000	0.435	0	0.00
Mn	3.105	0.681	0.0001	1.747	4.463
Fe	-4.535E-5	0.000	0.456	0	0.001

The mean iron level among preterm cases (94.5 ± 20.6) was significantly lower in comparison to mean among term group (147.9 ± 18.8) (p=0.0001).

However, as per acceptable iron level, all participant among both groups were fall in normal iron level range (Table 12).

Table 12: Iron level of studied groups

Iron Level	Preterm	Term	p-Value
Normal	40 (75%)	40 (97.5%)	-
Low	0	0	
Mean ± SD	94.5 ± 20.6	147.9 ± 18.8	0.0001*

*: independent sample t test.

The linear Regression analysis of the studied factors that associated with Iron showed that only Mn was associated with Iron level (Table 13).

Table 13: Iron level correlation with studied factors

Model	Unstandardized Coefficients		p-Value	95.0% Confidence Interval for B	
	B	St. Error		Lower bound	Upper bound
Age	0.74	0.517	0.157	-0.291	1.772
Hb	3.399	2.565	0.189	-1.713	8.511
BMI	0.38	1.078	0.725	-1.769	2.529
Cu	-0.602	0.256	0.021	-1.112	-0.093
Zn	0.019	0.313	0.953	-0.606	0.643
Mn	3763.578	1432.058	0.01	908.822	6618.33
Co	-170.484	227.616	0.456	-624.229	283.26

3. Discussion

Preterm birth is associated with a high degree of immature organs. Infants born preterm (before 37 completed weeks of gestation)31 are at greater risk of developing a range of short- and long-term comorbidities, especially lung dysplasia and infection.32 Furthermore, preterm birth and its complications account for 35% of all neonatal mortality and they further account for ~16% of deaths in children under 5 years old.33 By studying the factors that could affect the preterm birth, we could avoid or eliminate those risk factors and decrease the risk of preterm birth.

In this research, it was found that the average copper levels in the term group were notably lower when compared to the preterm group.

This observation aligns with a separate study conducted by Chiudzu et al., which also reported a connection between preterm birth and elevated copper concentrations in maternal serum.[8]

Furthermore, these findings exhibited lower copper levels when contrasted with the study conducted by Irwinda et al.[9], which documented higher levels at 215.35 µg/dL. Additionally, Irwinda et al. observed no significant distinction between the groups of women who experienced preterm births and those who carried pregnancies to full term. This disparity in results could potentially be attributed to variations in sample size, as Irwinda et al.'s study encompassed only 25 participants.[10]

Furthermore, an investigation conducted by Wang et al. revealed that pregnant women experiencing preterm labor exhibited serum copper concentrations similar to those of their counterparts. Notably, this study assessed copper levels during early pregnancy, specifically in the first trimester.[11]

In addition, Hao et al. conducted a study where they collected both plasma and serum samples during the initial prenatal

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visit, which occurred between the 4th and 22nd gestation weeks. Their findings indicated that, on average, maternal serum copper concentrations were significantly elevated in cases of preterm births when compared to births at full term within the Chinese population.[12]

Serum copper concentrations tend to rise during pregnancy due to the demands of the growing fetus and the physiological changes occurring in the mother's body. This increase in copper levels as pregnancy progresses can be attributed to heightened ceruloplasmin production, driven by elevated estrogen levels. Copper plays a crucial role in various enzyme systems, energy production, defense against oxidative stress, formation of connective tissue, and immune function.[13]

Moreover, it's expected that the premature birth group would exhibit higher copper levels. This is because copper accumulates to its maximum concentration in the mother's bloodstream by the end of the third trimester, with the intention of being delivered to the baby when the baby's liver is mature enough to handle it. In cases of prematurity, the infant's liver is not yet fully developed, preventing it from effectively storing and utilizing the copper present in the maternal blood.[14]

The average zinc levels in the preterm group were significantly lower than those in the term group. Additionally, there was a notable presence of participants in the preterm group who exhibited low zinc levels when compared to the term group.

Research exploring the connection between maternal serum zinc levels and preterm delivery indicated that low levels of zinc in maternal serum were linked to an increased risk of preterm delivery.[15] Furthermore, another study conducted by Zadrożna et al. reported an association between lower zinc levels and preterm pregnancies.[16]

On the contrary, a study led by Wang et al.[10] reported a different outcome, showing that maternal serum zinc concentrations were actually higher in women who had preterm births compared to those who gave birth at full term.

Additionally, their research indicated that a one-unit increase in zinc levels was associated with a seven-fold higher risk of experiencing a preterm birth. It's noteworthy that this particular study followed a prospective design, collecting samples during both the first and second trimesters.[17]

It's essential to acknowledge that some studies have not found any significant association between maternal zinc concentrations and preterm birth. These variations in findings could potentially be attributed to differences in the study population and the methodologies employed.[18]

The mechanism underlying the connection between higher maternal serum concentrations and an increased risk of preterm birth can be attributed to the dual role of zinc, functioning both as an antioxidant and a prooxidant, along with the cytotoxic effects of copper. The placenta serves as the primary source of reactive oxygen species (ROS).[19]

Nevertheless, the placenta possesses its own arsenal of antioxidants, including selenium-dependent enzymes such as glutathione dismutase, thioredoxin reductases, selenoprotein-P, and copper/zinc superoxide dismutase.

These enzymes rely on trace elements like selenium, copper, and zinc for their proper functioning. However, the elevated levels of free zinc and copper ions in women delivering prematurely might have led to the generation of ROS.[20]

Free zinc ions can inflict damage on mitochondria and NADPH oxidases, resulting in the production of ROS. Additionally, copper ions in their reduced form (Copper I) are also capable of independently generating ROS.[21]

Hence, the placenta plays a crucial role in generating reactive oxygen species. While ROS are necessary for certain physiological processes, their excessive production can be detrimental to both the mother and the developing fetus. The placenta is a significant source of ROS due to the oxygen-rich environment required for fetal development. The association between elevated maternal serum concentrations of zinc and copper and an increased risk of preterm birth may be attributed to the delicate balance of these trace elements' antioxidant and prooxidant functions. Disruptions in this balance can lead to the overproduction of reactive oxygen species, which may have adverse effects on the placenta and contribute to the onset of preterm labor.

In this study, the mean manganese level among preterm group was comparable to mean among term group with no significant difference between both groups.

This finding contrasts with a study conducted by Ashrap et al., which reported higher mean manganese concentrations in cases of preterm birth compared to births occurring at full term.[17]

Manganese is an essential nutrient with a critical role in the body, but excessive levels can be toxic.

These results are in line with reports of maternal and fetal toxicities associated with high-dose manganese intake and the observed U-shaped dose-response curve in both animal and epidemiological studies.[22] Moreover, another study conducted by Bakouei et al. found that manganese was the only micronutrient correlated with preterm delivery.[22] They further reported an association between high dietary manganese intake in pregnant women and an increased risk of preterm birth.

Manganese is recognized as an essential nutrient vital for both humans and animals. Its importance lies in its role in the development and maintenance of the skeletal system, the regulation of reproductive hormones, the activation of enzymes, and its ability to protect cells through its antioxidant properties.

However, it's worth noting that certain studies have pointed to potential toxic effects of elevated manganese levels on the developing fetus during pregnancy.[23]

The impact of manganese intake on fetal development and pregnancy outcomes has garnered attention in animal research. However, there is limited information available regarding the precise roles of manganese in human birth outcomes. Vigeh et al.[24] reported an association between blood manganese levels and the risk of intrauterine growth retardation (IUGR). In a cohort study conducted by Eum et al.[25] in Korea, it was observed that both extremely high and low maternal manganese levels were linked to lower birth weight outcomes.

Similarly, Zota et al.[26] identified a relationship between blood manganese levels and birth weight in a cohort consisting of 470 mother-infant pairs from Oklahoma.

The discrepancy in findings between studies underscores the complexity of manganese's role in pregnancy and preterm birth risk. While some studies suggest a correlation between higher manganese levels and preterm birth, others do not find a significant association.

The conflicting findings and potential health implications of manganese levels in pregnancy highlight the need for more comprehensive research. Future studies should aim to clarify the relationship between manganese, dietary intake, and preterm birth, taking into account various factors such as geographical location, dietary habits, and individual susceptibility.

Through an examination of cobalt levels, it was determined that the average cobalt level among preterm cases was significantly lower when compared to the average among term cases. When categorizing the cases based on the World Health Organization's normal values for cobalt, a noteworthy disparity emerged: a significantly higher proportion of patients exhibited lower cobalt levels among the preterm cases (25%) compared to the term cases (2.5%).

These findings align with the results of another study conducted by Li et al., which demonstrated that reduced levels of cobalt in maternal and umbilical cord serum were associated with an increased risk of preterm labor.[27]

There have been limited studies exploring the link between serum cobalt levels and the occurrence of preterm birth (PTB). A prospective study carried out in Korea did investigate this relationship and found that women with lower serum cobalt levels tended to have an elevated risk of preterm labor compared to those with normal serum cobalt levels. However, it's important to note that this particular finding did not reach statistical significance.[28]

Research has illuminated the potential of cobalt to influence oxidative stress and inflammatory responses.[29] Additionally, a separate study proposed a strong correlation between serum cobalt levels and the body's antioxidant status.[30] As a result, it becomes intriguing to hypothesize that higher concentrations of cobalt within the normal range might enhance blood flow to the placenta, subsequently reducing the harm caused by inflammatory and oxidative factors. 58

However, it's crucial to note that there is a paucity of studies delving deeply into this mechanism. As a result, we currently lack a comprehensive understanding of the precise effects. Further research endeavors are necessary to elucidate the intricate mechanisms at play in this context.

While there is evidence suggesting that cobalt within normal physiological ranges may play a role in modulating oxidative stress, inflammation, and placental health during pregnancy, the exact mechanisms remain a subject of ongoing investigation.

The average iron level among preterm cases was notably lower when compared to the average among the term group. Nevertheless, it's worth noting that when considering the acceptable iron level range, all participants in both groups fell within the normal range for iron levels.

Previous research has consistently affirmed that pregnant women experiencing iron deficiency face a significantly elevated risk of preterm birth. Furthermore, these studies have shown that the risk of preterm birth decreases as the duration of iron supplementation during pregnancy increases.[32]

In an American study conducted as part of the National Health and Nutrition Examination Survey (NHANES), it was observed that pregnant women showed a progressively higher prevalence of iron deficiency as pregnancy advanced through its trimesters.
During pregnancy, the demand for iron increases significantly because both the developing fetus and the placenta rely on iron for their growth and development.[33] Furthermore, in the third trimester, the expansion of maternal blood volume requires even more iron to support this process. The recommended daily intake of iron during pregnancy typically ranges from 1 to 1.5 mg/day, which can increase to as much as 5.0 mg/day during the second and third trimesters.

Despite these increased iron requirements, pregnant women may not always meet their nutritional needs adequately. It's not uncommon for pregnant women to consume only around 85% of the recommended dietary allowance for energy, and they often fall short in iron intake as well. This combination of a potentially poor-quality diet, insufficient intake, and the heightened nutrient requirements of pregnancy can lead to multiple micronutrient deficiencies, including iron deficiency.[34]

Iron deficiency in pregnancy can have detrimental effects. Research has shown a clear association between iron deficiency and an increased risk of preterm birth. When a pregnant woman lacks an adequate supply of iron, it can lead to complications such as anemia, which can negatively impact both maternal and fetal health. Hence, maintaining adequate iron levels during pregnancy is crucial for both maternal and fetal health. Iron deficiency during pregnancy is associated with an increased risk of preterm birth, likely due to its impact on oxygen transport, immune function, and inflammation.

In summary, the observed increase in maternal serum concentrations of some elements in women with preterm birth is consistent with the expected changes in trace element dynamics during pregnancy. This phenomenon underscores the intricate balance between maternal and fetal nutritional requirements and highlights the potential implications of altered trace element metabolism in the context of preterm birth. Further research with larger sample sizes could provide deeper insights into these relationships.

4. Conclusion

- Maternal blood Cobalt, Zinc, and Iron levels were significantly low among women with preterm birth in comparison to women with term birth.
- Copper level was significantly higher among women with preterm birth in comparison to women with term birth. However, majority of cases were fall with in normal range of Copper level.

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