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The Comparison Between Maternal and Umbilical Cord Blood Levels of Zinc and Copper in Active Labour Versus Elective Caesarean Section

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ABSTRACT

Background: Multivitamin administration in the periconceptional time was correlated with 16% decrement risk of premature deliveries. This study was aimed to investigate maternal and umbilical cord blood levels of zinc and copper in active labour versus elective caesarean.

Patients and Methods: A case-control study was carried out in Salah Al-deen general hospital form February to September 2020. The study included full term pregnant ladies with active labour or prepared for elective caesarean attending the labour unit in Salah Al-deen general hospital. A total of 60 full term pregnant ladies divided into two groups consist of: (30) women in active vaginal delivery women, and group of (30) women prepared for elective caesarean section. Trace elements' levels were evaluated utilizing the spectrophotometry.

Results: The mean maternal serum zinc level among vaginal delivery group was (87.45±14.99) µg/dL versus (87.84±13.8) µg/dL among caesarean group. The mean umbilical zinc level among vaginal delivery group was (90.34±22.56) µg/dL and was higher among caesarean group (88.8±31.9) µg/dL. The mean maternal serum copper level among vaginal delivery group (83.82±14.02) µg/dL was lower than among caesarean group (127.57±37.23) µg/dL.

Conclusion: There was higher mean umbilical cord zinc than the maternal zinc level. The mean umbilical cord zinc was lower than the maternal zinc among caesarean group. There was significantly lower mean umbilical cord copper than the maternal copper level among vaginal delivery group and the caesarean group. There was a positive significant correlation between maternal zinc level and umbilical zinc level. There was positive significant correlation between maternal copper level and umbilical copper level. Therefore, trace elements may play an essential function in the human parturition process.

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1. INTRODUCTION

Small amounts of trace elements are essential for proper bodily functions [1]. These elements play crucial roles in enzyme activity, protein transportation and storage, as well as signal transduction processes [1]. Copper (Cu) holds particular significance in myelin formation and upkeep [2], serving as a vital cofactor for enzymes like metalloproteinases, superoxide dismutase (SOD), catalase, and cytochrome oxidase [3]. Deficiency in copper can lead to vascular and nutritional disorders [3]. Zinc is indispensable for normal embryonic development, fetal growth, and protein synthesis [4-6]. Additionally, it provides protection against the harmful effects of excessive reactive oxygen species [7].

During pregnancy, the transportation of essential trace elements from the mother to the fetus varies, steadily increasing as the pregnancy progresses towards full term [2]. This transfer involves active transport for some elements across the placenta, while others are passively transported [8]. Inadequate trace elements negatively impact the health of both pregnant women and the developing fetus at this stage. Deficiencies in Zn, Cu, Mg, and Se have been linked to miscarriages, congenital disorders, and gestational abnormalities [8-10].

Although the precise mechanisms initiating labor remain unclear, the metabolic demands for both the mother and the fetus significantly rise during this stage [11]. Two general theories about human parturition are proposed: the pregnancy maintenance hypothesis and the uterotonin, prostaglandin, and oxytocin theory [11,12]. Consequently, understanding the mechanisms behind labor initiation is vital for both clinicians and researchers. The role of zinc and copper in the process of parturition has been relatively understudied [13].

1.2 Zinc
Zinc plays an essential function in the human body to help produce RNA, DNA and protein and to facilitate the stabilisation of the cellular membranes and the skeletal system[25,26]. Zinc is a cofactor for nearly (200) enzymes, including transferases, transplant passes, phosphatases and liver passages, thereby playing a major role in the functioning of the body in both immune system and antioxidant conditions. It's also important in the proper working of different hormones like insulin[27]. The daily needs range from (11) to (12) mg in pregnancy. Environmental sources include whole wheat bread, sausage, red meat, dried legumes, marine food and cheese. Studies have also documented that maternal zinc deficiency is prevalent, particularly in the developing world[28]. The researchers found a strong association between the amount of zinc of the maternal serum and the level of zinc in the mutated serum[29].

1.3 Copper
During pregnancy, females need approximately (1) mg of copper in a day[52]. Copper is rich in sunflower seeds, liver, dried legumes, chocolate, nuts, and oatmeal[52], it plays the major role in oxide residence processes, moreover, copper plays a major role in iron absorption and metabolism[53].
Since several essential enzymes work properly, the role for copper in the metabolism is crucial[54], it plays a significant role in maintaining the conjunctival tissue, skin, blood vessels endothelium[54]. It plays a positioning key for iron metabolism, production of hemoglobin, protective anti-oxidant properties, immune system functioning, melanin properties, and maintain proper functioning of thyroid[55-57].

1.4 Zinc and copper in pregnancy and mode of delivery
Minerals such as zinc, copper and other micro-nutrients impact pregnancy and the health of a developing fetus[72]. Spontaneous and congenital malformation were correlated with mother outcome of widespread zinc deprivation, but retaliation with intrauterine development and with weight relief in preterm delivery were also correlated with milder zinc outcome[73,74]. Moreover, low plasma zinc had been reported as linked to pregnancy complications such as hypertension, prolonged labour as well as postpartum bleeding [75]. Since pregnant women are considered to have been the highest risk arm for zinc deficiency, particularly in the developing world, in numerous trials the effect of zinc and copper on pregnancy were studied [76]. Some research focused more on maternal zinc and it was associated with bad outcomes in pregnancy, while others were interested in copper with correlations in expectancy and birth defects [77,78].

1.5 Aim of the study
This study was aimed to investigate maternal and umbilical cord blood levels of zinc and copper in active labor versus elective caesserean.

Objectives:
1- To investigate the difference in maternal and cord blood level of zinc among both study groups.
2- To investigate the difference in maternal and cord levels of copper among both study groups.
3- To identify the correlation between the maternal and cord blood levels of zinc.
4- To identify the correlation between the maternal and cord blood levels of copper.

2. PATIENTS AND METHODS
2.1 Study design:
A case-control study

2.2 Study area:
This research was carried out at department of obstetrics and gynecology in Salah Al-deen general hospital.

2.3 Study population
Full term pregnant ladies with active labour or prepared for elective cesarean, attending the labour unit in Salah Al-deen general hospital.

2.4 Time Data Collection: -
This clinical study was carried out in the period between February to September 2020.

2.5 Sample size
A total of (60) full term pregnant ladies divided into two group consist of (30) women in active vaginal delivery, and group of (30) women prepared for elective cesarean section.

2.6 Inclusion criteria:
1- Gestational age: women were at term gestation (37–41 completed weeks).
2- Singleton pregnancy.
3- Mothers with no medical disorder that might affect the results.
4- Newborns were ≥ 2500 g at birth.
5- No history of fetal problems or congenital anomalies

2.7 Exclusion criteria:
1- Gestational age: ≤ 36 week.
2- Multiple pregnancy.
3- Mothers with any medical disorder that might affect the results like diabetes and hypertension.
4- Newborns were < 2500 g at birth.
5- Any history of fetal problems or congenital anomalies.
6-Emergency caesarean section.

2.8 Data collection tools
The data were collected by the researcher using the following tools:
2.8.1 Questionnaire
A questionnaire was prepared by the researcher for collecting data concerning; age, gestational age, and level of education, residency, and history of systemic diseases (hypertension, and DM).

A thourough medical & obstetric history was taken from each pregnant females (e.g.: age, parity, medical disorders before or during pregnancy).

2.8.2 Physical examination

General physical clinical examination and specific abdominal examination were done for each pregnant female, Ultrasound report for each pregnant lady has been checked in the study.

2.8.3 Laboratory investigations

a- Blood Sample

(5) ml of blood had been drawn from mothers before delivery in both groups.

(5) ml of blood had been drawn from umbilical cord after delivery immediately.

b- Zinc and Copper assay

(5) ml of blood was taken (maternal and cord) and not allowed to clot, centrifuged at (2500) rpm for (15) min at room temperature to obtain serum which was stored at (-20) °C. Zinc and copper assessment were done using the colorimetric test with Dibromo-PAESA(spectrophotometry).

2.9 Data processing and analysis

Data analysis and interpretation done using Statistical Package for Social Sciences (SPSS) version (25). Data presented using Mean and proportions by which the comparison done between normal vaginal delivery group and elective cesarean delivery. Statistical analysis done using Student's t test and chisequare test p < (0.05) was considered significant.

2.10. Ethical consideration:

- Agreement of Iraqi ministry of health, and Salah Al-deen directorate of health.
- The collection of data was kept confidential and not be divulged except for the purpose of the study.
- The Participant's agreement was considered and they informed that the participation is voluntary and they can withdraw from the study after having agreed to participate.
- A written informed consent from each participant was obtained after explaining the study objectives and prior to the start of data collection.

3. RESULTS

3.1. The general characteristics of the study sample

The mean age of women with vaginal delivery was (26.83±5.6) with median of(25.5), while of the caesarean section was (28.0±2.9) with median of (27.5). The commonest age was < 35 years, among vaginal delivery it includes (27) patients (90%), and 28 patients (93.3%) in caesarean section group, this relation was statistically not significant.

Regarding the parity, most of the vaginal delivery group patients had either (0) parity [(7) patients (23.3%)], (1-2) parity, [(10) patients (33.3%)], (3-4) parity, [(10) patients (33.3%)] and only (3) patients (10%) had ≥ (5) parity, meanwhile in caesarean section group, (7) patients (23.3%) had (0) parity, (16) patients (53.3%) had (1-2) parity, (5) patients (16.7%) had a parity of (3-4), and only (2) patients (6.7%) had a parity of ≥ (5). This relation was statistically not significant, as shown in table 3.1.

Most of vaginal delivery and C/S group had no previous abortion, (26) patients (86.7%) of vaginal delivery group and (27) patients (90%) of caesarean section group had (0) previous abortions , this relation was statistically not significant, as shown in table 3.1.The mean gestational age was (38.37 ± 1.01) among vaginal delivery group, while caesarean section group was (38.7 ± 0.76), this relation was statistically not significant, as shown in table 3.1.

Table 3.1. The general characteristics of the study groups

Parity	Vaginal delivery Group		Elective Caesarian section Group		Total		P value
	Frequency	Percent	Frequency	Percent	Frequency	Percent	
Age < 35 ≥ 35	26.83 ± 5.6		28.0 ± 2.9				
	27	90%	28	93.3%	55	91.7%	> 0.05 NS*
	3	10%	2	6.7%	5	8.3%	
Parity 0 1_2 3_4 ≥ 5							
	7	23.3%	7	23.3%	14	23.3%	> 0.05 NS**
	10	33.3%	16	53.3%	26	43.3%	
	10	33.3%	5	16.7%	15	25.0%	
	3	10%	2	6.7%	5	8.3%	

Abortion 0							
	26	86.7%	27	90%	53	88.3%	> 0.05 NS**
1-2	3	10%	3	10%	6	10%	
≥2	1	3.3%	0	0.0%	1	1.7%	
Gestational age in wks.	38.37 ± 1.01		38.7 ± 0.76				>0.05 NS***

* Fisher's Exact Test, P value>0.05 not significant.

** Likelihood Ratio test =3.298, P value >0.05 not significant.

*** student t-test p value >0.05 Not significant.

3.2. The maternal and umbilical Zinc level analysis

The mean maternal Serum zinc level among vaginal delivery group was (87.45±14.99) µg/dL versus (87.84 ± 13.8) µg/dL among caesarean section group this relation was statistically not significant (p value > 0.05). The mean umbilical zinc level among vaginal delivery group was (90.34 ± 22.56) µg/dL which was higher than among caesarean section group (88.8 ± 31.9) µg/dL, this relation was statistically significant (p value < 0.05). In comparision between the maternal Serum zinc, and umbilical cord zinc in, there was higher mean umbilical cord zinc than the maternal zinc level in both groups, this relation was statistically not significant as shown in table 3.2.

Table 3.2. The maternal and umbilical zinc level analysis

	VD Group	Group C/S	
	Mean ±SD	Mean ±SD	P value*
Maternal Serum zinc µg /dL	87.45 ± 14.99	87.84 ± 13.8	0.91
Umbilical cord zinc µg /dL	90.34 ± 22.56	88.8 ± 31.9	0.001*
P value*	0.78	0.56	

*Student t-test

3.3. The maternal and umbilical Copper level analysis

The mean maternal serum copper level among vaginal delivery group (83.82 ± 14.02) µg/dL was lower than among caesarean section group (127.57±37.23) µg/dL, this relation was statistically significant (p value < 0.05). The mean umbilical copper level among vaginal delivery group was (73.33 ± 19.7) µg/dL was lower than among caesarean section group (107.84 ± 32.18) µg/dL, this relation was statistically significant (p value < 0.05). In comparision between the maternal serum copper, and umbilical cord copper, there was significantly lower mean umbilical cord copper than the maternal copper level among vaginal delivery group and the caesarean section group. These relations were statistically significant as shown in table 3.3.

Table 3.3. The maternal and umbilical copper level analysis

	VD Group	**Group (C/S)**	
	Mean ± SD	Mean ± SD	**p value***
Maternal Serum Copper µg/dL	83.82 ± 14.02	127.57 ± 37.23	0.0001*
Umbilical cord Copper µg/dL	73.33 ± 19.7	107.84 ± 32.18	0.0001*
p value*	0.032*	0.029*	

*student t-test

3.4. The correlation between maternal and cord zinc and copper

There were positive significant correlation bettween maternal zinc level and umblical zinc level(r = 0.37), and between maternal copper level and umblical copper level(r = 0.66) , as shown in table 3.4. and figure 3.1.

Table 3.4. The Pearson correlation between cord and maternal zinc & copper.

	Maternal Serum zinc		Maternal Serum copper		Umbilical cord zinc	
	r	P value	r	P value	R	P value
Maternal Serum copper	0.073	0.58	1		0.11	0.42
Umbilical cord zinc	0.37 **	0.008	0.11	0.42	1	
Umbilical cord copper	-0.01	0.943	0.66 **	0.0001*	0.158	0.227

**. Correlation is significant at the 0.01 level (2-tailed).

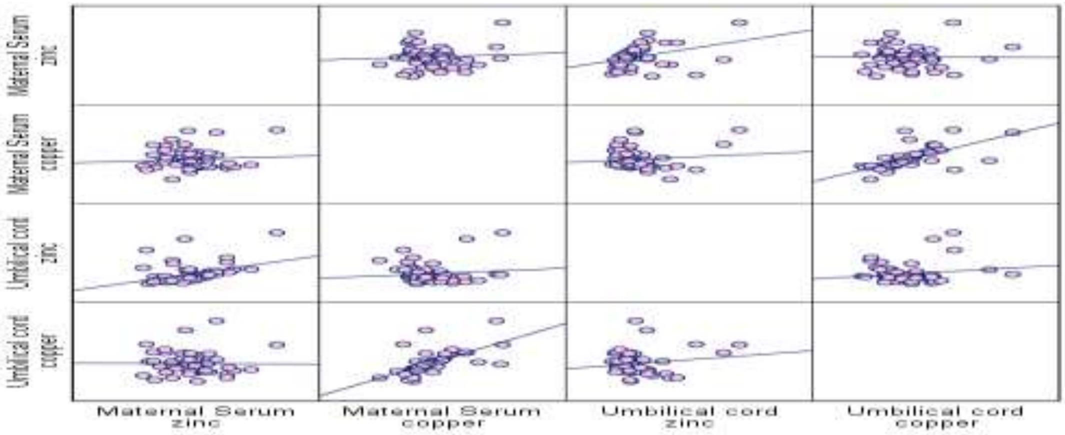

Fig 3.1. The correlation between cord and maternal zinc and copper.

The commonest indication for caesarean section delivery was previous caesarean section ≥ 2 (17) patients, (56.7%), followed by fetal distress (5)patients (16.7%), malpresentation (3)patients(10%), placenta previa (2)patients (6.7%), macrosomia (2)patients (6.7%), and precious baby (1)patient(3.3%), as shown by figure 3.2

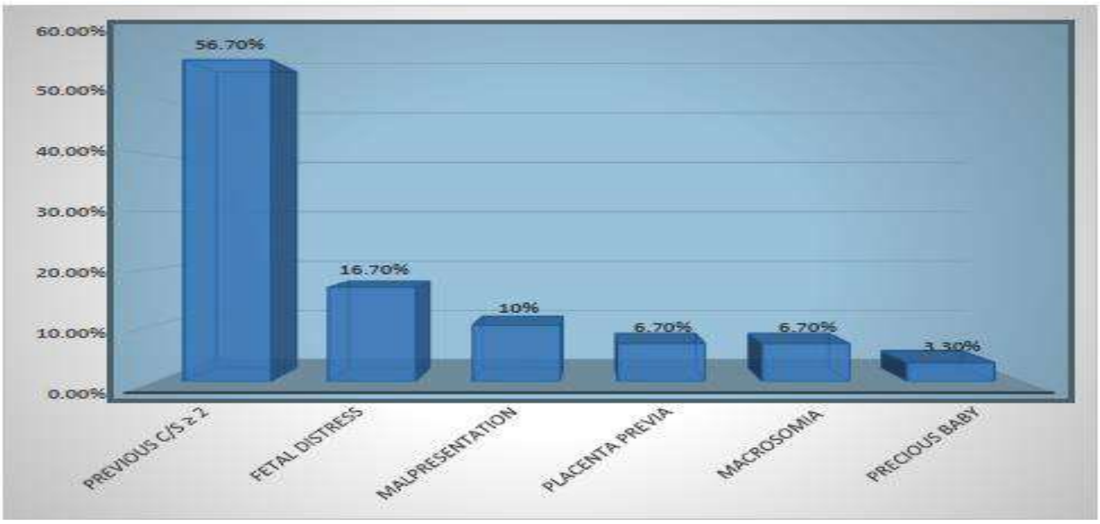

Figure 3.2. The main indications of caesarean section.

4. DISCUSSION

4.1. General Characteristics of the Study Sample

Our study revealed that the mean age of women with vaginal delivery was (26.83±5.6) with median of (25.5), while of the caesarean section group was (28.0±2.9) with median of (27.5). Our study revealed that the mean gestational age was (38.37±1.01) among vaginal delivery group, while caesarean section group was (38.7±0.76), this is relatively similar to results found by a study held by Elhadi A et al, which found that the mean age of women with vaginal delivery was (28.1±4.6) while of the caesarean section group was (29.2±4.1), and found that the mean gestational age was (38.5±1) among vaginal delivery group, while in caesarean section group was (38.8 ± 1)[80].

Regarding the parity, this study revealed that the most of the vaginal delivery group had (1-2), (3-4) babies and most of caesarean section group had (1-2), this finding was also concurrence with Elhadi A et al study which revealed similar results[80].

This study revealed that the commonest age of patients was <(35) years among vaginal delivery and caesarean section groups,this finding was concurrence with S.M. Awadallah et al study which found that the mean age of patients was 27 ± 4.9 years[81].

This study found that the most of vaginal delivery and caesarean section group had no previous abortion which was concurrence with Ofakunrin AOD et al study[82].

4.2. Maternal and Umbilical Zinc Level Analysis

This study revealed that the mean maternal Serum zinc level among vaginal delivery group was (87.45±14.99) µg/dL versus (87.84 ± 13.8) µg/dL among caesarean section group in a statistically not significant relation (p value > 0.05). This is differing from a study carried by Rafal Kocylowski et al, which showed a significant reduction was found in the zinc concentrations post-delivery in maternal serum in vaginal delivery group compared to caessarean group[83]. This difference can be explained by the fact that in the latter study, they took blood and fluid loss during or after delivery and dehydration as a possible causative factor.

The current study results also disagree with the results were found by Khawla AH et al study, which found significantly increase in zinc concentrations in maternal blood serum of normal vaginal delivery group versus caesarean section group. This may explained by the fact that zinc is essential for proper growth of fetus and the fall in zinc during pregnancy could also be a physiological response to expanded maternal blood volume[84].

Our results are also different from the results of a study held by Lazer et al which found that both elements zinc and copper concentrations were significantly elevated in normal vaginal delivery group compared to cesarean section group[85].

This study revealed that the mean umbilical zinc level among vaginal delivery group (90.34±22.56) µg/dL was significantly higher than that among caesarean section group (88.8±31.9) µg/dL (p value < 0.05), which similar to Elhadi A et al results (mean umbilical zinc level among vaginal delivery group (97.8) µg/dL was significantly higher than that among caesarean section group (81.5) µg/dL)[80].

In comparision between the maternal serum zinc, and umbilical cord zinc, there was non-significant higher mean umbilical cord zinc than the maternal zinc level in vaginal delivery group, while the mean umbilical cord zinc was higher than the maternal zinc among caessarean section group in statistically non-significant relation. This might be explained by Wang H. et al study which found that the presence of cadimum polution prevents zinc transfer from mother to the fetus[86].

4.3. The maternal and umbilical Copper level analysis

This study revealed that the mean maternal serum copper level among vaginal delivery group (83.82±14.02) µg/dL was significantly lower than that of caessarean section group (127.57±37.23) µg/dL. The same found by Elhadi A et al study which revealed that the mean maternal serum copper level among vaginal delivery group (78.8) µg/dL was significantly lower than that of caessarean section group (92.4) µg / dL[82]. This study also revealed that the mean umbilical copper level among vaginal delivery group was (73.33±19.7) µg/dL was significantly lower than that of caessarean section group (107.84 ± 32.18) µg/dL and this finding was in contrast to Elhadi A et al who found that the mean umbilical copper level among vaginal delivery group was (43.5) µg/dL was significantly higher than that of caessarean section group (32.2) µg/dL[82].

In line with the findings of Elhadi A et al., the present study demonstrated notably decreased levels of maternal and cord zinc, as well as cord copper, in women who underwent vaginal delivery when compared to those who had a caesarean delivery [82]. When comparing maternal serum copper with umbilical cord copper, a significantly lower average level of umbilical cord copper was observed in the vaginal delivery group and the caesarean section group. Lazer T et al.'s investigation also discovered significantly elevated levels of copper in the umbilical cord vein in cases of vaginal delivery compared to caesarean delivery. This study additionally highlighted considerable variations in trace element concentrations in fetal blood during active labor versus elective caesarean section. These findings suggest that trace elements may play a pivotal role in the process of human parturition [84]. Baig, N. U. Hasnain, and Q. Ud-din's research indicated an increase in copper concentration during the final three months of pregnancy, followed by a decrease after delivery [87].

4.4. Correlation between Maternal and Cord Zinc and Copper

This study revealed that there was positive significant correlation bettween maternal zinc level and umblical zinc level (r = 0.37), and between maternal copper level and umblical copper level (r = 0.66). Baig, N. U carried out a study in Pakistan in 2003 found a positive correlation was observed between zinc and copper in maternal and cord blood[87]. This is differing from a study of Rafał and Kocyłowski et al found higher levels of zinc and also lower levels of copper in umbilical cord blood than in maternal serum.[83] Iwai-Shimada carried out a study in Japan on 2019, found that placental zinc concentrations was significantly higher than those in the maternal and cord blood, and also found that the variations of the copper, zinc were small [25–55%][88].

4.5 Caessarean Section Indications

This study revealed that the commonest indication was Previous caessarean section ≥ 2, followed by fetal distress, malpresentation, placenta previa, macrosomia, and precious baby, this finding was concurrence with a study held by H. Ahmed and N. Al-Tawil carried a study in Erbil, Iraq and revealed that the major general indications for cesarean section were a previous cesarean section (70.49%), cephalopelvic disproportion (35.31%) and mother's request (14.26%)[89]. Maysoon Jabir study stated that the previous two caessarean section or more are considered as absolute indications for caessarean section in Iraq[90]

5. CONCLUSIONS

1. There was higher mean Umbilical cord zinc than the maternal zinc level.
2. The mean Umbilical cord zinc was higher than the maternal zinc among caessarean section group.
3. There was significantly lower mean Umbilical cord copper than the maternal copper level among vaginal delivery group and the caessarean section group.
4. There were positive significant correlation bettween maternal zinc level and umblical zinc level (r = 0.37).
5. Ther were positive significant correlation between maternal copper level and umblical copper level (r= 0.66).
6. The main indications of cesarean section was previous caessarean section ≥2 , followed by fetal distress, malpresentation, placenta previa, macrosomia, and precious baby.

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