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Original Research Article

Maternal Micronutrient Alterations Associated with *Pseudomonas aeruginosa* Infection Following Cesarean and Vaginal Delivery

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Abstract: ***Background:*** There is micronutrients including vitamin D, zinc, and iron which are important as they are involved in immune regulation, control of inflammatory conditions, and defence of the host against bacterial infections. *Pseudomonas aeruginosa* is a Gram-negative opportunistic pathogen and is able to take advantage of host micronutrient imbalances by using nutritional immunity mechanisms. The physiological stress and inflammatory reaction that may occur after the birth of a child can cause postpartum women, especially following cesarean section, to have an impact on micronutrient status. Nevertheless, there is not much information on the joint effect of delivery mode and P. aeruginosa infection on the biochemical profiles of the mothers. ***Aim:*** The aim of the study was to compare the impacts of the type of delivery and confirmed infection of *Pseudomonas aeruginosa* infection on serum levels of 25-hydroxyvitamin D, zinc, iron, and calcium in women aged 3045 years in Thi-Qar Governorate, Iraq. ***Methods:*** The study involved a comparative cross-sectional study that was controlled and used a total of 400 study participants split into four groups (n=100 each): CS+INF (cesarean section with infection), CS-INF (cesarean section without infection), VD + INF (vaginal delivery with infection), and VD-INF (vaginal delivery without infection). All participants with the infection were confirmed by laboratory tests to have P. aeruginosa infection. Women who have chronic illnesses or are currently on micronutrient supplementation were not allowed. Blood samples (venous blood) were collected and serum 25 (OH)D (ng/mL), zinc (mu g/dL), iron (mu g/dL), and total calcium (mg/dL) measured. Data were presented as the means and SD and measured with the help of the Two-Way ANOVA to evaluate the impact on infection status and delivery mode, as well as their interaction. A p-value less than 0.05 was taken to be statistically significant. ***Results*** The concentration of vitamin D, zinc, and iron was significantly lower among the infected groups than the non-infected groups. The lowest levels were always in the CS+INF group (25(OH)D: 13.5 +5.5 ng/mL; zinc: 69 +12 ug/dl; iron: 47 +18 ug/dl). Vaginal delivery in an uninfected (VD-INF) status had the most micronutrient level (25(OH)D: 24.0 ± 8.0 ng/mL; zinc: 92 ± 15 µg/dL; iron: 85 ± 25 µg/dL). Iron level was found to be affected by both infection and mode of delivery whereas those of vitamin D and zinc were related mostly to the state of infection. There was very little difference in total calcium levels between groups and all were within the physiological ranges of reference. ***Conclusions:*** *Pseudomonas aeruginosa* infection is linked to massive losses in the levels of serum vitamin D, zinc and iron amongst women who have given birth. Cesarean birth could also contribute to iron deficiency, probably because of a combination of both the inflammatory and surgical conditions. Calcium homeostasis does not seem to be affected. The given findings underscore the need to monitor micronutrient status of postpartum women who had an infected past especially those who undergo cesarean section in order to promote immune functioning and recovery.

Keywords: Pseudomonas aeruginosa; Cesarean section; Vitamin D; Zinc; Iron; Micronutrients; Postpartum infection; Inflammation.

1. INTRODUCTION

Micronutrients are essential in keeping the immune system fit and in controlling inflammatory reactions. Vitamin D, zinc, and iron are among them, and they are especially important to the host defense mechanism against bacterial pathogens. Deprivation of

these micronutrients has also been linked to poor innate and adaptive immune response, vulnerability to infection, and slow healing of inflammatory diseases [1,2]. Reduced immune balance in this population is particularly susceptible to the effects of pregnancy and the postpartum period because of the physiological demands of these processes in reproductive-aged wome)[3].

The vitamin D is becoming more and more known as immunomodulatory hormone but not just a calcium metabolism regulator. It promotes the production of antimicrobial peptides, such as cathelicidin and defensins, which are needed to protect against Gram-negative bacteria through the activation of the vitamin D receptor (VDR) [4,5]. Reduced 25-hydroxyvitamin D [25(OH)D] in circulation has been linked to an enhanced risk and severity of infectious diseases especially those involving the respiratory and systemic infection by bacteria [6].

Zinc is a crucial trace element that takes part in over 300 enzymatic processes and is required when it comes to lymphocyte growth, cytokine management, and oxidative stress [7]. When the host gets infected, the body triggers a response in the form of nutritional immunity, which is a defense response that redistributes zinc and other transition metals to restrain access by microbes [8]. Nonetheless, chronic redistribution or an underlying deficiency can impair the efficiency of immune systems and slow down the elimination of bacteria.[9]

The metabolism of iron is strictly controlled in case of infection because of a dual role of this element in the physiology of the host and microbes' development. Production of hepcidin is stimulated by inflammatory cytokines, which causes the macrophage sequestration of iron and low serum iron levels- anemia of inflammation [10,11]. Although such a reaction restricts bacterial growth, it can also negatively affect oxygen delivery and tissue healing, especially in postpartum women who can already be iron deficient because of the loss of blood.[12]

Pseudomonas aeruginosa is a Gram-negative opportunistic pathogen that can cause infections of wounds, infections of the urinary tract, and postoperative complications. It has also advanced metal-acquisition systems that help it to compete with host nutritional immunity systems, especially that of zinc and iron [13,14]. The elderly women, particularly those delivering through cesarean section, are particularly vulnerable to infection caused by surgical trauma, exposure at the hospital, and temporary immunological changes.[15]

Cesarean section is also related to increased inflammatory response and increased blood loss than vaginal section which can affect maternal biochemical parameters [16]. Although the role of micronutrients in immune defensive mechanism is acknowledged, there is little study on the synergistic impact of mode of delivery and the proven *Pseudomonas aeruginosa* infection on the micronutrient status of the maternal state. The aim of the study was the determination of the impact of delivery type and confirmed *Pseudomonas aeruginosa* infection on serum levels of 25-hydroxy vitate D, and the levels of zinc, iron, calcium among women aged (3045) years in Thi-Qar Governorate, Iraq.

2. MATERIALS AND METHODS

Study Design and Setting

This was a controlled comparative cross-sectional study in Thi-Qar Governorate, Iraq, to determine the biochemical effect of delivery mode and *Pseudomonas aeruginosa* infection among 30-45 years old women. The research participants compared the groups of cesarean sections and vaginal delivery with and without confirmed infection with an aim of determining independent and interactive effects on the chosen parameters of micronutrients.

Collection of the sample and Biochemical Testing.

Venous blood (5mL) were collected under aseptic conditions. Serum was centrifuged and examined on standard laboratory procedures based on manufacturer directions. The biochemical markers assessed were 25-hydroxyvitamin D [25(OH)D], serum zinc, serum iron and total serum calcium determined by quantitative validated assays.

Statistical Analysis

The data were presented in terms of mean standard deviation (Mean ± SD). Two-Way ANOVA was used to determine the independent effects of the type of delivery and infection status, and the interaction. The statistical significance was set at p below 0.05.

3. RESULTS

The current research has shown that the mode of delivery and the *Pseudomonas aeruginosa* infection have a definite impact on the choice of biochemical parameters.

Vitamin D [25(OH)D]

The serum 25(OH)D concentration in infected groups was significantly less in comparison with the non-infected groups (CS+INF: 13.5 ± 5.5 ng/mL; VD+INF: 15.8 ± 6.0 ng/mL). The least concentration was in the CS+INF group.

This result implies that infection status has significant relationships with the low levels of vitamin D. The further decrease in the group of cesarean-infected people might indicate joint physiological stresses of surgery and infection. The effect of vitamin D deficiency is more evident in the infected participants irrespective of the method of delivery.

Serum Zinc

Zinc levels in serum were the same. The level of zinc in infected groups was less (CS+INF: 69 ± 12 µg/dL; VD+INF: 71 ± 12 µg/dL) than in non-infected groups (CS-INF: 87 ± 14 µg/dL; VD-INF: 92 ± 15 µg/dL).

This means that infection has a great impact on zinc state. The loss of Zinc in the infected participants is the same in both types of delivery and infection-free vaginal delivery exhibited the highest zinc levels. The impact of infection is found to be stronger than that of mode of delivery.

Serum Iron

The lowest level of serum iron was in CS+INF (47 + 18 µg/dl), then VD+INF (56 + 20 µg/dl), CS-INF (71 + 22 µg/dl), and VD-INF (85 + 25 µg/dl).

The level of iron unlike vitamin D and zinc seems to be affected by infection as well as the type of delivery. The significant decrease of the CS+INF group indicates the interaction of the perioperative blood loss and inflammatory response. The best iron profile was revealed by vaginal delivery and infection-free delivery.

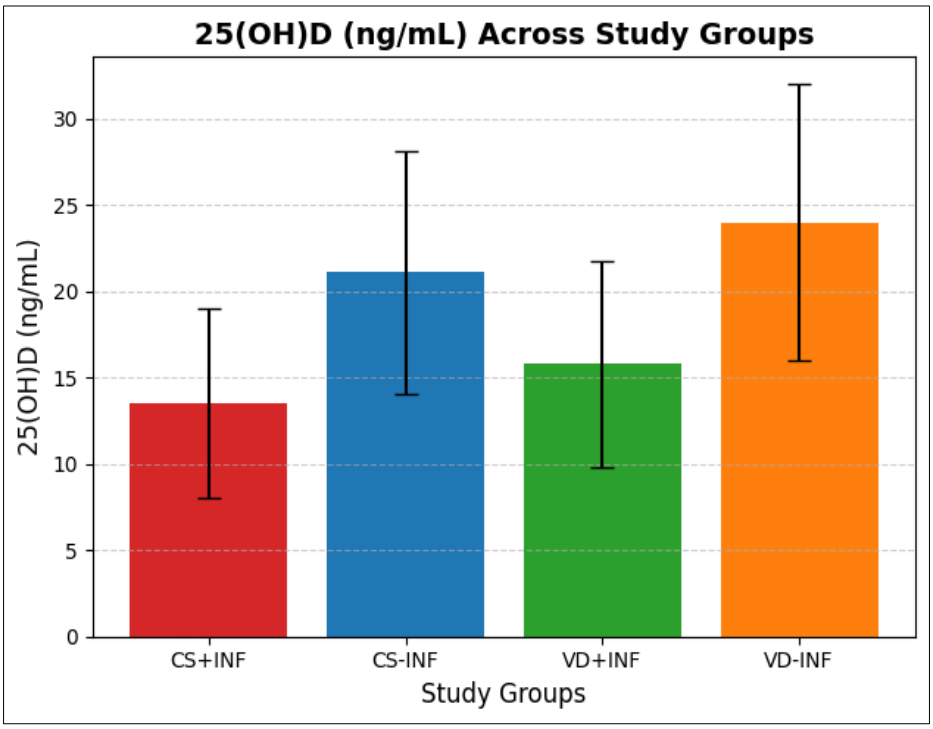
Total Calcium

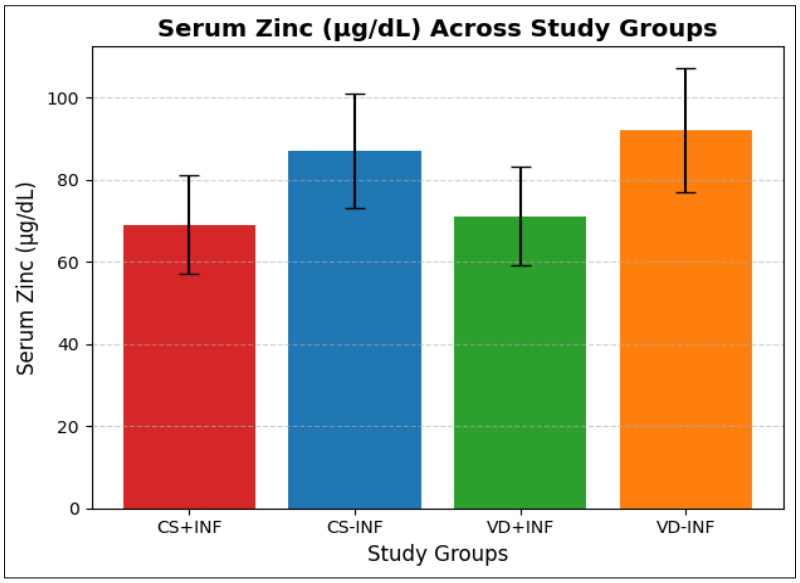
There was little variation in total serum calcium by groups (range: 8.8 9.2mg/dl). Despite the fact that the values were slightly lower with infected groups, all the measurements were within the physiological reference range.

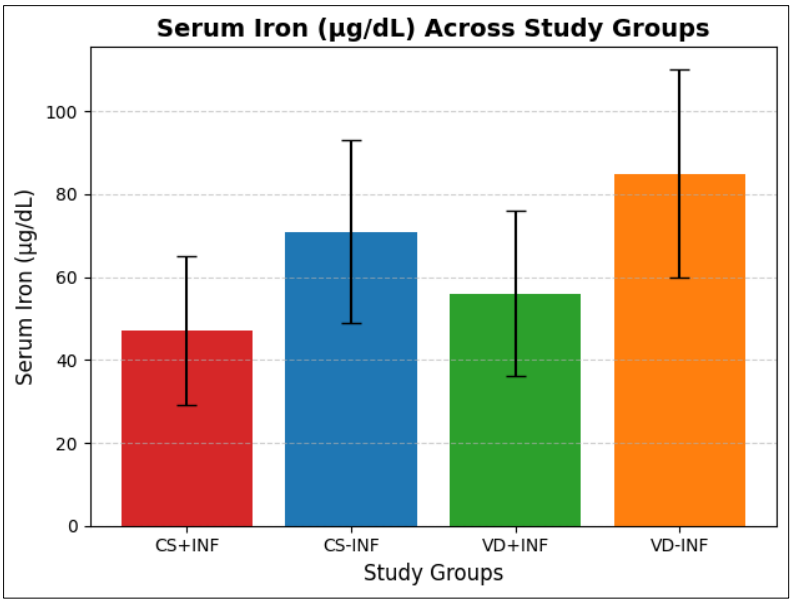
It shows that the calcium homeostasis is rather stable and not influenced by both types of infections and delivery as vitamin D, zinc, and iron.

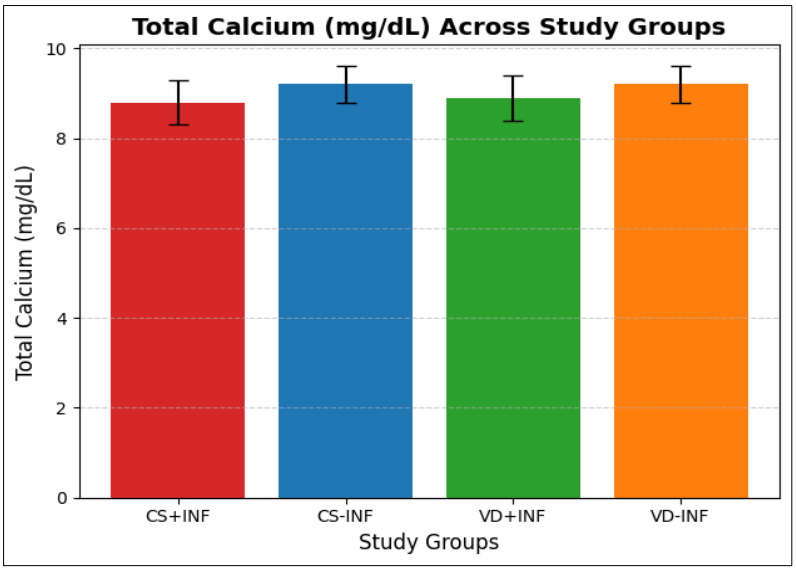
Table 1: Biochemical Characteristics of the Study Population based on the Type of Delivery and the Infection of *Pseudomonas aeruginosa*

Parameter	CS+INF	CS-INF	VD+INF	VD-INF
25(OH)D (ng/mL)	13.5 ± 5.5	21.1 ± 7.0	15.8 ± 6.0	24.0 ± 8.0
Serum Zinc (µg/dL)	69 ± 12	87 ± 14	71 ± 12	92 ± 15
Serum Iron (µg/dL)	47 ± 18	71 ± 22	56± 20	85 ± 25
Total Calcium (mg/dL)	8.8 ± 0.5	9.2 ± 0.4	8.9 ± 0.5	9.2 ± 0.4




Serum Zinc (µg/dL) Across Study Groups
Serum Zinc (µg/dL)
0
20
40
60
80
100
CS+INF
CS-INF
VD+INF
VD-INF
Study Groups


Serum Iron (µg/dL) Across Study Groups
Serum Iron (µg/dL)
0
20
40
60
80
100
CS+INF
CS-INF
VD+INF
VD-INF
Study Groups


Total Calcium (mg/dL) Across Study Groups
Total Calcium (mg/dL)
0
2
4
6
8
10
CS+INF
CS-INF
VD+INF
VD-INF
Study Groups

4. DISCUSSION

This current research shows that *Pseudomonas aeruginosa* infection is linked with a great decrease in serum levels of 25-hydroxyvitamin D, zinc, and iron and a comparatively constant level of total calcium. Besides, cesarean delivery seems to predispose iron depletion especially to infected women. These results point to the interplay of infection-induced inflammatory processes, redistribution of micronutrients, and surgical stress.

Vitamin D has a major immunomodulatory effect by activating the vitamin D receptor (VDR), which controls the expression of antimicrobial peptides, including cathelicidin (LL-37) and 8-defensins [18]. These peptides help to maintain the integrity of the epithelial barrier and guide the antimicrobial action against Gram-negative microbes, such as P. aeruginosa. The limitation of serum 25(OH)D in the participants who are infected might thus affect the innate immune defenses and compromises against bacterial clearance.

In addition, the inflammatory cytokines like IL-6 and TNF-a that are increased during bacterial infections can also override the levels of circulating vitamin D by modifying hepatic metabolism and increasing its intake during immune response [19]. The significantly reduced vitamin D concentrations in the CS+INF group could be a result of combined action of perioperative physiological stress and an effect of infection-induced inflammation. It is known that surgical trauma provokes acute phase responses that temporarily alter the micronutrient metabolism.[20]

Zinc is necessary in the thymic action, lymphocyte expansion, and the control of oxidative stress [21]. When infected, the host develops a nutritional immunity response, which diets zinc out of the plasma by increasing the level of zinc-binding proteins, e.g. metallothioneins [22]. This hyperacute redistribution decreases extracellular zinc levels to invading pathogens but also decreases measured serum zinc levels. Notably, P. aeruginosa boasts of very effective zinc acquisition mechanisms (e.g., ZnuABC transporters), making it compete with host zinc in the event of infection [23]. This pathogenesis is in the form of host-pathogen competition, which can contribute to zinc depletion in the infected individual. Our results of a steady decrease in zinc in both infected groups does not refute the hypothesis that infection status is the key determinant of zinc decrease and not the mode of delivery.

Iron metabolism is deeply altered in case of infection. The hepatic synthesis of hepcidin is stimulated by inflammatory signals, especially IL-6, preventing the macrophages and enterocytes to export iron through ferroportin [24]. This process decreases the circulating iron levels, restricting access of microbes but possibly causing functional iron deficiency or anemia of inflammation [25]. The least iron concentrations were found in the CS+INF group, which implies that inflammatory iron binding and perioperative blood loss have an additive effect. The Cesarean section is also linked to more blood loss than vaginal delivery hence iron depletion may be increased further [26]. Thus, it seems that both inflammatory processes induced by infections and physiological factors associated with delivery lead to iron status in this cohort.

Contrary to the other measured parameters, total serum calcium was found to be within normal limits of physiological parameters in all the groups. The mechanisms of calcium homeostasis are strictly controlled by parathyroid hormone, calcitonin, and vitamin-D programs [27]. There is no evidence of pronounced hypocalcemia, and so, it is possible that even short-term infection and surgical stress can not severely interfere with the systemic regulation of calcium in women without chronic illness in otherwise good health.

5. CONCLUSIONS

In this study concluded that the Pseudomonas *aeruginosa* infection is closely correlated with the low serum levels of vitamin D, zinc, and iron among postpartum women who are aged between 30 and 45 years, irrespective of the mode of delivery. The strongest deficiencies were seen in women that experienced cesarean section and were infected implying a mixed interaction of inflammatory reactions and surgical stress. Iron depletion seems to be caused by both sequestration due to inflammation and perioperative blood loss. Conversely, the loss of vitamin D and zinc was mostly associated with the state of infection, which is also the case with the vitamins since they play a significant part in immune response and host defense. Total serum calcium was kept within normal ranges, which signified that the system is in a consistent condition of regulation. The results indicate that monitoring and treating micronutrient deficiencies in infected postpartum women should be monitored and corrected to aid in immune functioning and recovery, which needs to be followed up by longitudinal studies.

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