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DIETARY VITAMIN E AMELIORATES ZINC-TISSUE CONCENTRATION IN ZINC-DEFICIENT PREGNANT RATS

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ABSTRACT

Zinc is an essential nutritional trace element whose activity promotes various vital functions in the body. Further, vitamin E, α-tocopherol, is a potent antioxidant against oxidative stress and changes in tissue mineral content. Thus, the present study was aimed to investigate the beneficial role of vitamin E in improving zinc tissue concentration in rats fed a zinc-deficient diet. Forty pregnant rats were equally divided into four animal groups (n=10), received respectively, adequate zinc-diet (54mg/kg diet; Control G1); zinc-deficient diet (1mg/kg; G2); adequate zinc plus vitamin E supplemented diet (54mg zinc + 500mg vitamin E/kg; G3); and zinc-deficient diet plus and vitamin E (1mg zinc + 500mg vitamin E/kg; G4) over 21 days. Zinc deficiency caused decreased body weight gain, food intake, and concentration of zinc in kidney, liver, and femur tissues excluding the pancreas. Consequently, the insufficiency of dietary zinc levels in pregnant rats decreases zinc tissue concentration in the placenta and fetus.

KEYWORDS:
Zinc Deficiency, Pregnancy, Vitamin E, Reproduction, Rats

INTRODUCTION

Trace elements or trace minerals are essentially found at low concentrations in nature and living organisms (less than 0.01% of the organism weight), although of their importance in various physiological and metabolic processes occurring within living tissues [1-3]. Zinc is one of the most important trace elements contributing to some molecular structures in the body, including enzymes (cofactor for over 300 enzymes) and nearly 2000 transcription factors [4], in addition to many biological functions (eg, protein synthesis, cell division and nucleic acid metabolism [5]). Additionally, zinc promotes fertility, embryo development, fetal maturation, child growth, intellectual development and immunity, healing, and maintenance of the bone matrix [6].

It also acts as an efficient antioxidant in the non-enzymatic cell structures and leads to delay in the antioxidant protein induction, such as metallothioneins [7, 8]. Several previous studies have reported a direct relationship between zinc deficiency, fetal growth restriction, and fetal malformations [9], evidencing thus that the preservation of zinc balance is of critical importance in avoiding the possible consequences of low zinc levels on pre- and post-natal life. Insufficient quantities of zinc during embryogenesis may influence the final phenotype of all organs. Maternal zinc restriction during pregnancy influences fetal growth, while adequate zinc supplementation during pregnancy may result in a reduction of the preterm birth risk [10].

It has been reported also that some pathophysiological conditions resulting in oxidative stress-mediated reactive oxygen species (ROS) generation are able to alter the zinc tissue concentration, as well as obesity can cause zinc deficiency, and subsequently oxidative tissue damages, and cell death and diseases accompanied by alterations in the antioxidant defense systems [11,12].

The latter include enzymatic antioxidants (e.g catalase, superoxide dismutase, and glutathione peroxidase) and non-enzymatic antioxidants evidenced mainly by glutathione; an abundant peptide that can be oxidized by glutathione peroxidase can be effectively deactivated. In addition, some natural exogenous substances like tocopherols (vitamin E), carotenoids, ascorbic acid, flavonoids, and tannins are considered as efficient non-enzymatic able to attenuate the oxidative stress effects [13,14].

Vitamin E is a powerful antioxidant scavenging free radicals (FR), and was first discovered in 1922 as a vital substance for reproduction, and accordingly, it was extensively studied and has become widely used owed to its powerful lipid-soluble antioxidant and anticancer activity. The biological activities of vitamin E, including roles in anti-proliferation, anti-survival, pro-apoptotic, cancer anti-angiogenesis therapy, and anti-inflammation have been well documented. There are various

reports on the benefits of vitamin E on health in general [15].

However, up to now, the biological effect of vitamin E on reproduction is poorly elucidated. This paper was written to provide a review of the known roles of vitamin E as an antioxidant in female reproductive health. Very limited research studies investigating the effect of vitamin E on zinc deficiency mediated oxidative tissue injuries in experimental animals [16,17] have reported that vitamin E supplemented diet is effectively able to reduce the effect of zinc deficiency resulting in oxidative tissue damages via free radicals generation causing oxidation of cell macromolecules (lipids, proteins, and nucleic acids). Therefore, the present study was designed to investigate the beneficial effect of dietary vitamin E on zinc tissue concentration in zinc-deficient pregnant albino rats.

MATERIALS AND METHODS

Animals. Forty adult female albino rats weighing between 180 and 210g were used. The animals were obtained from the Pasteur Institute of Algiers, Algeria. They were housed in polypropylene cages with free access to food and water and maintained during two weeks before the study at room temperature (22 ± 2°C), relative humidity of 40%, and 12/12 hour light/dark cycle. All experimental procedures were approved by the Animal Care Committee and Ethics Committee of our institution (AFRO. No 478, 2009).

Experimental Design. Animals were used at the pregnancy stage and divided equally into 4 groups as the control group and treated groups: Group 1 (G1), rats fed a diet containing adequate zinc level (54mg zinc/kg diet, control group); group 2 (G2), rats fed on a zinc-deficient diet (1mg zinc/kg diet) [18]; group 3 (G3), rats fed vitamin E plus adequate zinc supplemented diet (54mg zinc + 500mg of vitamin E/kg diet) [8]; group 4 (G4), rats fed zinc-deficient diet plus vitamin E (500mg vitamin E/kg and 1mg zinc/kg) [19]. Bodyweight and food intake of control and experimental rats were measured every day during the last ten days of the experimental treatment. Thereafter, animals of all groups were sacrificed by decapitation and subsequently, liver, kidney, pancreas, femur, fetus, and placenta were immediately removed, washed in 9 % sodium chloride solution (NaCl), weighed, and dried at 80°C for 16 hours for determination of zinc tissue concentration.

TABLE 1
Body weight gain (g) and food intake (g diet/ day) in control and experimental groups.

	G1	G2	G3	G4
Body weight gain (g)		**Mean ± SD**		
	16,39± 0,97	11,31± 1,48****	17,1± 0,85 NS	14,96± 1,38*
Food intake (g / d)	21,87± 1,71	18,05± 1,21****	21,32± 1,886 NS	20,36± 1,06*

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

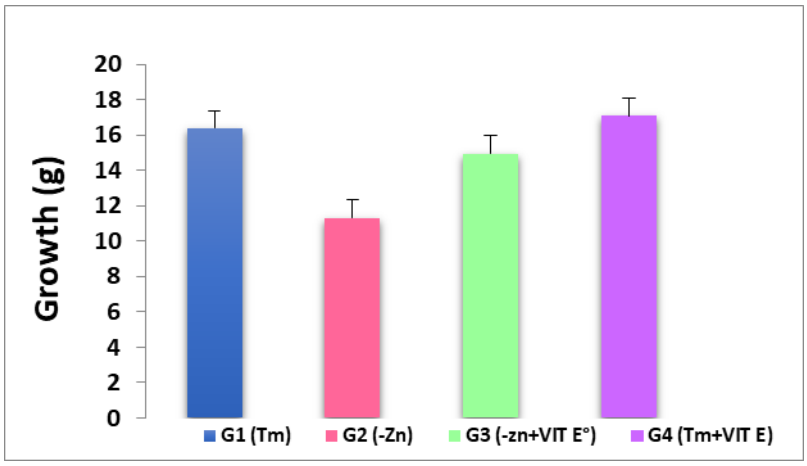

FIGURE 1
Bodyweight gain in pregnant rats

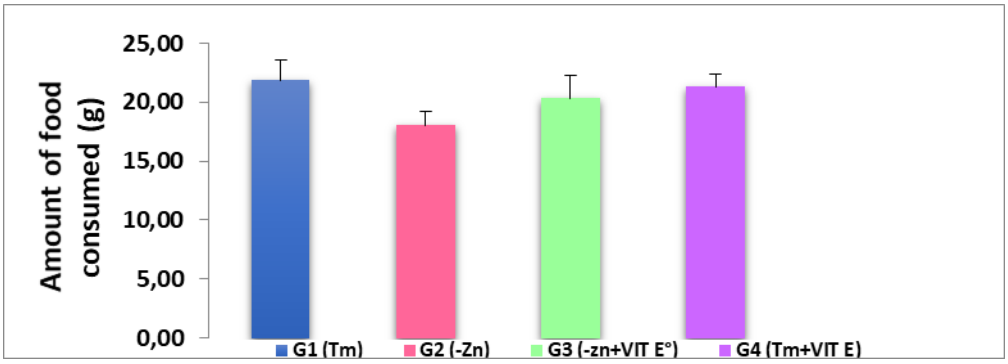

FIGURE 2
Food intake in control and experimental pregnant rats

Determination of Zinc Tissue Concentration. The dried organs were dry-mineralized in a muffle furnace at 458°C for 48 hours. Then, samples were washed, dissolved in 10 ml of 1 M HNO3, and filtered using filter paper (Whatman No. 542). The tissue zinc content in the prepared mineralizes (after dilution with HNO3) in the samples (after dilution wither distilled water) were measured by atomic absorption spectrophotometry (ICP-AES) at Materials Research Unit, Nanomaterials and Ecosystems, Faculty of Sciences of Bizerte, University of Carthage (Tunisia) as described elsewhere [20]. The obtained values of zinc concentration were compared with a standard guideline of zinc nitrate concentration (1 mg/ml) provided in the same conditions.

Statistical analysis. The data were given as Mean ± SD and pairwise comparisons were tested for statistical significance by unpaired Student's t-test. Statistical tests were performed using Minitab software (Ver, 14, 0) where $p < 0.05$ was considered significant [21].

RESULTS

As shown in Table 1, Figure 1 and 2, body gain and food intake were highly significantly decreased ($P < 0.0001$) in rats fed a zinc-deficient diet (G2) as compared with control-diet (G1), since rats fed zinc deficiency and vitamin E supplemented diet (G4) revealed significant increase ($P < 0.05$) in these parameters as compared with rats fed zinc deficiency diet (G2).

Table 2 and Figure 3 revealed a highly significant decrease ($P < 0.0001$) in zinc liver concentration of rats fed zinc No significant difference was noticed in rats fed a normal diet plus vitamin E (G3) and those fed zinc deficiency diet plus vitamin E (G4).

Zinc tissue concentration showed a highly significant ($P<0,0001$) decrease in rats fed a zinc deficiency diet, a long with a highly significant increase in the group treated with a normal diet and supplemented with the control diet-rats. No significant difference between control group(G1) and G3 was noticed (Table3, Figure4).

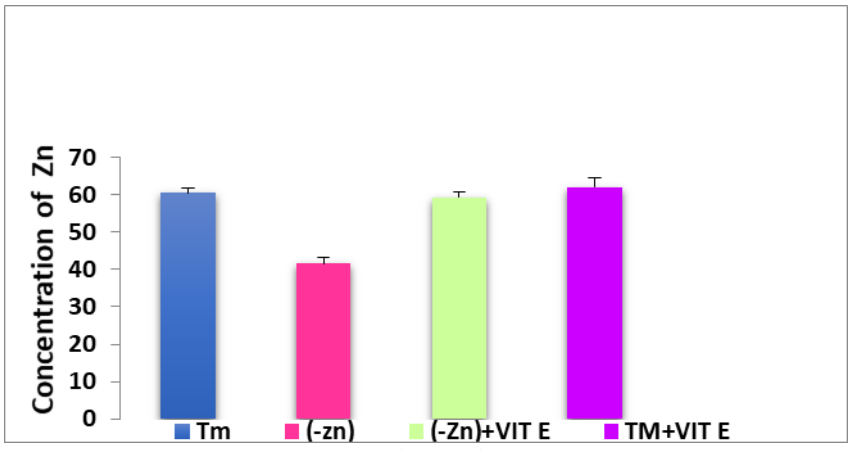

FIGURE 3
Zinc tissue concentration in the liver

TABLE 2
Fresh and dry liver weights (g), water content (%), and tissue zinc concentration (µg / g) in the liver of control and experimental groups.

	Liver			
	G1	G2	G3	G4

	Mean ± SD			
Fresh weight (g)	3,552± 0.46	4,486± 0.34****	3,57± 0.37 NS	3,31± 0.29 NS
Dry weight (g)	1,001± 0,22	1,352± 0,28**	0,98± 0,22 NS	0,99± 0,18 NS
Water content (%)	28,5± 0,69	25,34± 0,69****	29,4± 1,20 NS	28,55± 0,42 NS
Zinc tissue concentration (µg/g)	60,64± 1,36	41,64± 1,59****	62,2± 2,43 NS	59,39± 1,42 NS

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

TABLE 3
Fresh weight (g), dry weight (g), water content (%), and zinc tissue concentration (µg / g) in the kidney of control and experimental groups

	Kidney			
	G1	**G2**	**G3**	**G4**
	Mean ± SD			
Fresh weight (g)	0,90± 0,05	1,12± 0,11****	0,91± 0,05 NS	0,967± 0,10 NS
Dry weight (g)	0,20± 0,12	0,39± 0,05***	0,22± 0,01 NS	0,20± 0,03 NS
Water content (%)	28,33± 0,99	26,18± 0,25****	30,2± 1,89*	28,4± 2,26 NS
Zinc tissue concentration (µg/g)	164,6± 5,56	84,87± 4,36****	183,8± 3,80****	165,9± 6,45 NS

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: rats fed on diet composed of adequate zinc level + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: rats fed on zinc deficiency diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n=10 rats / group).

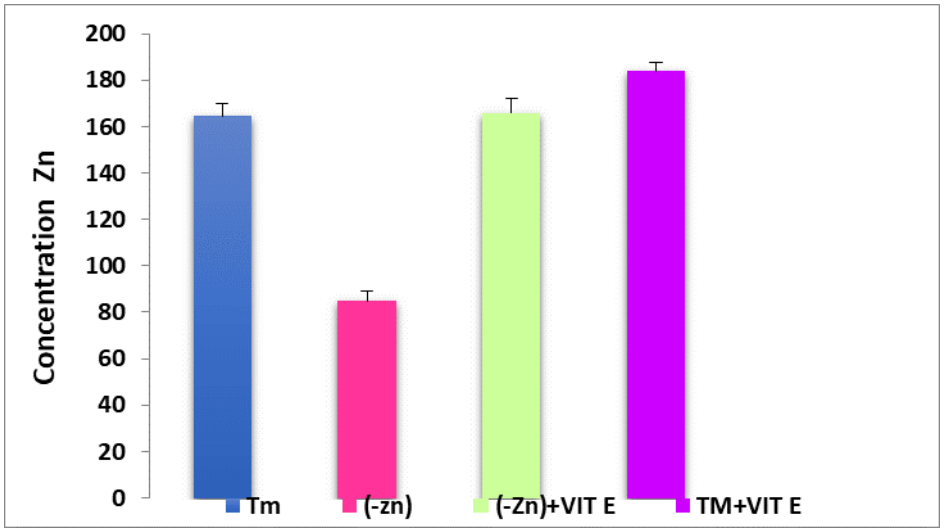

FIGURE 4
Zinc tissue concentration in the kidney

TABLE 4
Fresh weight (g), dry weight (g), water content (%), and zinc tissue concentration (µg / g) in the pancreas of control and experimental groups

	Pancreas			
	G1	**G2**	**G3**	**G3**
	Mean ± SD			

Fresh weight (g)	0,59± 0,03	0,48± 0,075***	0,68± 0,175 NS	0,64± 0,15 NS
Dry weight (g)	0,41± 0,04	0,33± 0,04**	0,48± 0,13 NS	0,45± 0,15 NS
Water content (%)	61,41± 1,44	58,65± 3,327*	69,4± 1,75****	55,92± 3,45***
Zinc tissue concentration (µg/g)	50,62± 2,32	146,3± 3,54****	62,67± 2,32****	52,07± 6,68 NS

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

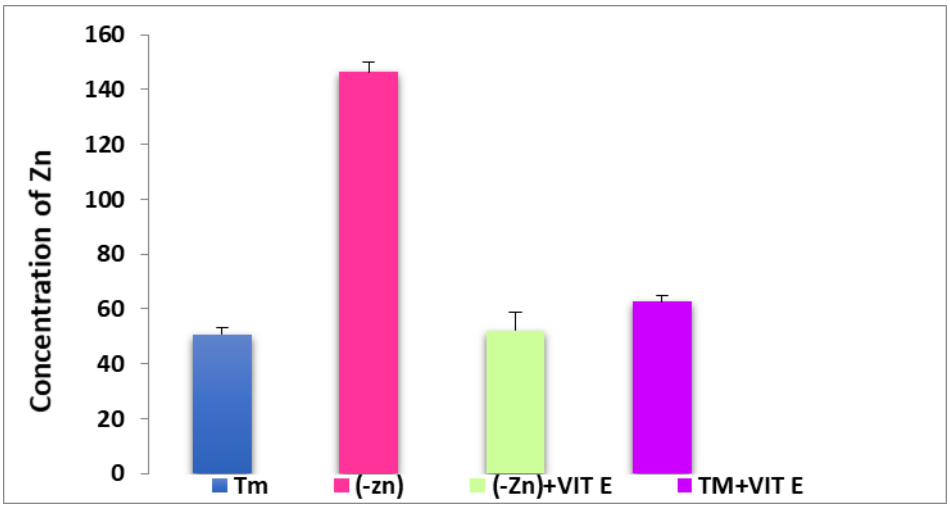

FIGURE 5
Zinc tissue concentration in the pancreas

TABLE 5
Fresh weight (g), dry weight (g), water content (%), and zinc tissue concentration (µg / g) in the femur of control and experimental groups

	Femur			
	G1	**G2**	**G3**	**G4**
	Mean ± SD			
Fresh weight (g)	0,89± 0,07	1,109*± 0,30	1,01± 0,26 NS	0,91± 0,04 NS
Dry weight (g)	0,61± 0,06	0,764± 0,07***	0,63± 0,02 NS	0,60± 0,04 NS
Water content (%)	37,64±0,91	72,77± 4,70****	40,22± 1,98**	40,69± 2,26***
Zinc tissue concentration (µg/g)	157,6±3,67	90,78± 3,62****	156,9± 1,19 NS	170± 8,56***

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

TABLE 6
Fresh weight (g), dry weight (g), water content (%), and zinc tissue concentration (µg / g) in the fetus of control and experimental groups

	Fetus			
	G1	**G2**	**G3**	**G4**
	Mean ± SD			
Fresh weight (g)	3,56±0,45	1,99±0,29****	3,3±0,43 NS	3,85±0,46 NS

Dry weight (g)	1,2±0,04	0,10±0,02****	1,05±0,30 NS	1,58±0,05****
Water Content (%)	20,43±2,29	40,52±1,69****	22±3,14 NS	21,82±1,55 NS
Zinc tissue concentration (µg/g)	138,63±1,70	88,03±4***	140,60±2,03*	42,37±2,88**

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

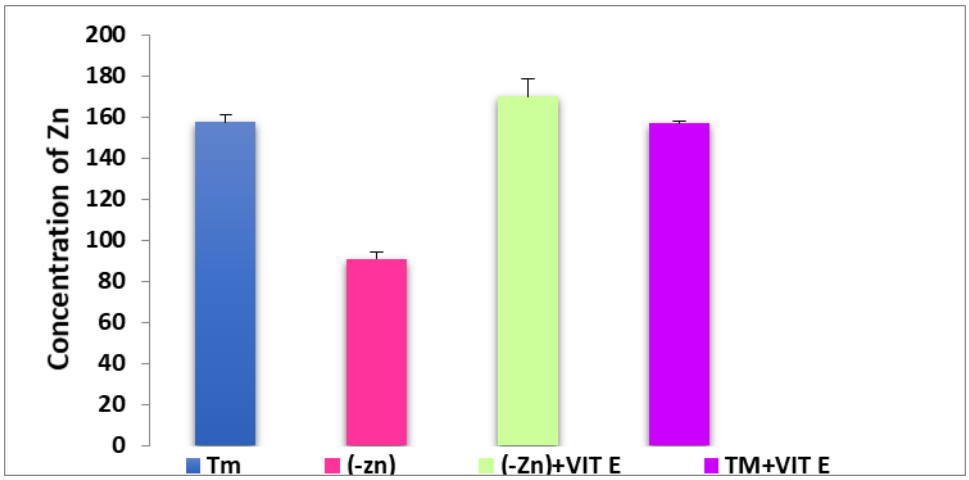

FIGURE 6
Zinc tissue concentration in the femur

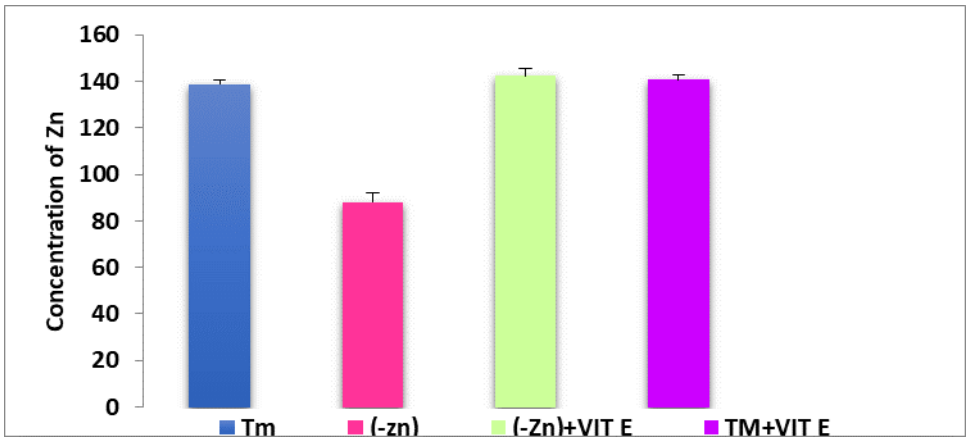

FIGURE 7
Zinc tissue concentration in the fetus

TABLE 7
Fresh weight (g), dry weight (g), water content (%), and zinc tissue concentration (µg / g) in the placenta of control and experimental groups

	Placenta			
	G1	**G2**	**G3**	**G4**
	(Mean ± SD)			
Fresh weight (g)	1,08±0,13	1,12±0,15 NS	1±0,23 NS	0,99±0,29 NS
Dry weight(g)	0,84±0,06	0,77±0,10 NS	0,81±0,02 NS	0,09±0,02****
Water content (%)	70,94±1,14	74,45±5,84 NS	72,39±1,98 NS	70,47±2,19 NS
Zinc tissue concnetration (µg/g)	190,5±5,96	92,65±6,14****	193,9±4,80 NS	187,1±5,52 NS

G1: Control diet rats (54mg zinc/kg diet); G2: Zn- deficient rats (1mg zinc/kg diet); G3: adequate zinc + vitamin E (54mg zinc + 500mg vitamin E/kg diet); G4: zinc deficient diet + vitamin E (1mg zinc + 500mg vitamin E/kg diet) (n= 10 rats/group).

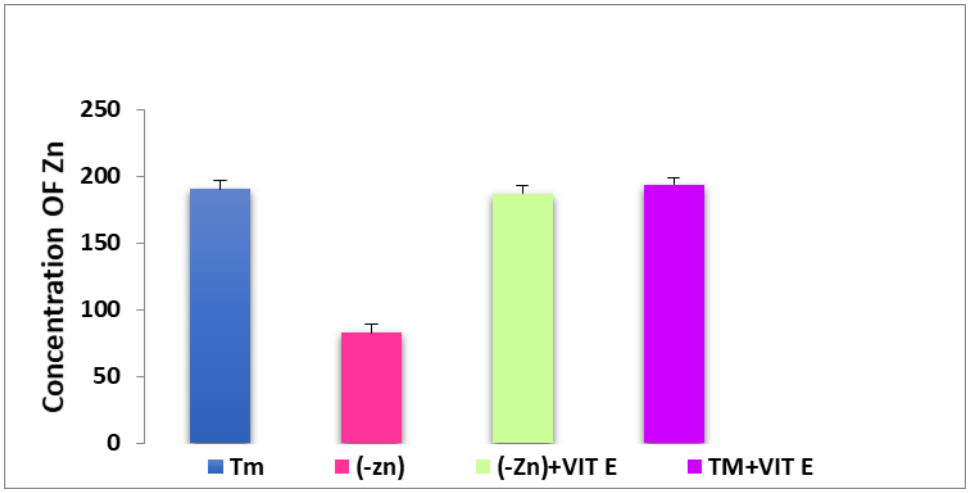

FIGURE 8
Zinc tissue concentration in the placenta

As shown in Table 4 and Figure 5, a highly significant (P<0.0001) decrease in zinc tissue concentration in the pancreas was observed in rats fed zinc deficiency diet, and a highly significant increase in rats receiving adequate zinc diet plus vitamin E as compared with the control diet rats. No significant difference in zinc concentration was noticed in a zinc-deficient diet plus vitamin E.

A highly significant (P <0.0001) decrease in zinc concentration in the femur was noticed in rats fed zinc deficiency diet (G2) as compared with control diet rats (G1), whereas no significant differences were noticed in rats fed adequate zinc level with vitamin E supplemented diet (G3) and those fed zinc deficiency diet plus vitamin E (G4) (Table 5, Figure 6).

Table 6 and Figure 7 reveal a highly significant (P <0.0001) decrease in zinc tissue concentration in the fœtus of rats fed a zinc deficiency diet (G2) as compared with control diet rats. No significant difference was noticed in rats fed an adequate zinc diet plus vitamin E (G3) and those fed zinc deficiency diet plus vitamin E (G4).

The results shown in Table 7 and Figure 8 reveal a highly significant (P<0.0001) decrease in zinc tissue concentration in the placenta of rats fed a zinc deficiency diet (G2) as compared with control-diet rats (G1), since rats fed a combination of adequate zinc and vitamin E (G3) and those fed zinc deficiency diet plus vitamin E did not show any significant differences.

DISCUSSION

Owing to the importance of nutritional zinc in fetal development, growth, and immune function, zinc insufficiency in food during pregnancy may lead to serious teratogenic effects which can be effectively reduced by exogenous antioxidants, including vitamin E [22, 23].

Therefore, the present study was devoted to investigating the beneficial role of vitamin E supplemented diet in attenuating the effect of zinc deficiency on zinc tissue concentration in the main target organs of pregnant female rats. In this study, a marked decrease in body weight gain and food intake was noticed in rats receiving zinc-deficiency diet (G2) as compared with those fed adequate dietary zinc (G1) and, in this regard, the same findings were previously reported [24, 25].

Furthermore, zinc deficiency is able to induce anorexia in humans and animals through the central role of zinc in activating many enzymes involved in the synthesis and breakdown of biologically active peptides commonly known as neuropeptides, contributing to the regulation of food intake [26-28].

Also, the pituitary gland modulating food intake receives metabolic signals and, subsequently transmits them to other target peripheral tissues or organs [29, 30]. Zinc deficient diet in many animal species leads to serious digestive disorders associated with lack of appetite, bodyweight loss, and growth retardation resulting mainly from the deterioration of taste and smell [31, 32].

On the other hand, vitamin E-treated pregnant rats were found to increase food intake and body weight [33]. In the present study, zinc deficiency caused a marked decrease in zinc concentration in the main target organs: liver, kidney, and femur. This finding is in line with that found by [34] and [35] suggesting the strong relationship of the zinc concentration in tissue and the diet.

Unlike other organs, the pancreas showed an increase in zinc tissue concentration proving thus its high sensibility to variation in zinc dietary intake [36]. Herein, the experimental animals exhibit an effective mechanism for retaining zinc from the body through homeostatic reaction according to the increased needs of low zinc dietary intake. This mechanism leads to increased zinc tissue concentration in the pancreas of zinc-deficient diet, although

its concentration is fifty times lower than that in rats fed a normal diet.

It is well-documented, that animals and humans receiving low dietary minerals are often able to retain zinc and other minerals found in some of their tissues, even in the state of severe deficiency [37]. The results revealed also a significant increase in the concentration of zinc in the studied organs of pregnant rats receiving adequate zinc and vitamin E supplemented diet. This is in agreement with the results of [38] who proved the effect of vitamin E in improving zinc tissue concentration in tests in lead intoxicated rats.

Conversely, zinc deficiency showed a significant decrease in zinc tissue concentration in the placenta and fetus of pregnant rats in comparison with those fed a normal zinc diet (G1), and this may be related to the low maternal zinc received by fetus and placenta under dietary zinc deficiency [35]. Other studies have shown that maternal zinc deficiency has long-term effects on the growth, immunity, and metabolic state of offspring [39, 40]. Additionally, previous studies using experimental animals such as rats, mice, pigs, and ewes showed that severe zinc deficiency increases fetal death due to spontaneous abortions or multiple birth defects [41], including organ malformations evidenced by abnormal synthesis of nucleic acids and proteins, decreased cell growth and morphogenesis, abnormal tubulin polymerization, chromosomal defects and excessive lipid peroxidation of cell membranes.

CONCLUSION

Conclusively, vitamin E has effectively improved body weight loss, decreased food intake, and zinc tissue concentration in liver, kidney, femur, placenta, and fetus in zinc-deficient rats. Thus, a zinc-deficient diet proved to be able to disrupt growth rate, dietary intake, and zinc status in vital tissues of pregnant rats, meanwhile vitamin E can act as a powerful antioxidant in attenuating generation of free radicals leading to a decrease of Intracellular zinc concentration.

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REFERENCES

[1] Mehri, A., Marjan, R.F. (2013) Trace Elements in Human Nutrition: A. Review. Int. J. Medinvest. 2 (3), 115-128.

[2] Beausir, A., Kim, I., Séguy, D., Michaud, L., Lannoy, D. (2011) Micronutrients in parenteral nutrition The Hospital Monitor. 238, 15-28.

[3] Bhattacharya, P., Satya Ranjan., M, Mohsina, H. (2016) Nutritional Aspects of Essential Trace Elements in Oral Health and Disease. An Extensive Review. J. Sci. 2012 pages.

[4] Marreiro, D., Cruz, K.J.C., Morais, J.B.S., Beserra, J.B., Severo, J.S., Oliveira, R.S. (2017) Zinc and Oxidative Stress: Current Mechanisms. Antioxidants. 6(24), 1-9.

[5] Chaffee, B.W., King ,J.C. (2012) Effect of Zinc Supplementation on Pregnancy and Infant Outcomes.A Systematic Review.Paediatr Perinat Epidemiol. 26(01), 118-137.

[6] Girodon, F., Galan, P., Monget, A.L., Boutron-Ruault, M.C., Brunet-Lecompte, P., Preziosi, P., Arnaud, J., Manuguerra, J.C., Herchberg, S. (1999) Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients. A randomized controlled trial. Arch. Intern. Med. 159, 748-754.

[7] Sidhu, P., Garg, M.L., Dhawan, D.K .(2004) Protective effects of zinc on oxidative stress enzymes in liver of protein deficient rats. Nutr. Hosp. 19(6) ,341-347.

[8] Miao, X., Wang, Y. (2013) Zinc protects against diabetes-induced pathogenic changes in the aorta: Roles of metallothionein and nuclear factor (erythroid-derived 2)-like 2. Cardiovasc. Diabetol. 12- 54.

[9] Norrozi, M., Borna, S., Parichehr, H., Soghrat, F., Fedyeh, H., Shokoufeh, G .(2012) Evaluation of Zinc Supplementation Effect on Fetal Outcomes in Pregnant Women with Lower-than-Median Serum Zinc Concentration. J. Fam. Repr .Hea. 6(2), 85 – 89.

[10] Terrin, G., Bernicanani, R., Chiara, M., Pietravalle ,A., Aleandri ,V., Conte ,F., De curtis , M. (2015) Zinc in early life: akeyelement in the fetus and preterm neonate. Nutrients. 11, 7(12), 10427-10446 .

[11] Martins, L.M., Oliveira, A.R.S. (2014) Influence of cortisol on zinc metabolism in morbidly obese women. Nutr. Hosp. 29, 57–63.

[12] Sulibuska, J., Bogdanski, P. (2014) Changes in mineral status are associated with improvements in insulin sensitivity in obese patients followingL-arginine supplementation. Eur. J. Nutr. 53, 387–393.

[13] You, H.J., KIM, J.Y., Jeong ,H.G. (2003) 17 beta-estradiol increases inducible nitricoxide synthase expression in macrophages. Biochem. Biophys. Res. Commun. 303(17), 1129-1134.

[14] Naskar, S., Islam, A., Mazumder, U.K., Saha, P., Haldar, P.K., Gupta, M. (2010) *In Vitro* and *In Vivo* Antioxidant Potential of Hydromethanolic Extract of Phoenix dactylifera Fruits. J. Sci. Res. 2(1), 144-157.

[15] Siti Syairah, M.M., Sharaniza, A., Mohd Hamim , R.(2018) Vitamin E as an Antioxidant in Female Reproductive Health. Anti. J. 7(2), 22 .
[16] Kinalski, M., Śledziewski, A., Telejko, B., Zarzycki, W., Kinalska , I. (2000) Lipid peroxidation and scavenging enzyme activity in streptozotocin-induced diabetes. Acta-Diabetologica. 37 (4), 179-183 .
[17] Evans, J.L. (2007) Antioxidants: do they have a role in the treatment of insulin resistance .Ind. J. Med. Res. 125 (3), 355.
[18] Southon, S., Kechrid, Z., Wright, A.J.A., Fairweather-Tait, S. (1988) Effect of reduced dietary zinc intake on carbohydrate and zinc metabolism in the genetically diabetic mouse (C57BL/KsJdb+/db+). Brit. Nutr. 60 (3), 499-507.
[19] Demiralay, R,,Gürsan, N., Erdem, H. (2007) Regulation of nicotine-induced apoptosis of ulmonary artery endothelial cells by treatment of N-acetylcysteine and vitamin E. Hum. Exp. Toxicol. 26 (7), 595-602.
[20] Southon, S., Gee, J., Johnson, I.T. (1984) Hexose transport and mucosal morphology in the small intestine of the zinc-deficient rat. Brit. Nutr. 58, 371-380.
[21] Dagnelie, P.(1999) Theoretical and appliquation. Tome 2 statistics: statistical references to one and two dimensions. Brussels. Univ. of Boeck and Larcier. 659 Pp.
[22] Keen, C.L., Taubeneek, M.W., Daston, G.P., Rogers, J.M., Gershwin, M.F. (1993) Primary and factors underlying abnormal CNS development. Annals of New York Academy of Sciences. 678, 37-47.
[23] Vallee, B.L., Falchuk, K.H. (1993) The biochemical basis of zinc physiology. Physiol Rev. 73, 79-118.
[24] Kechrid, Z., Hamdi, M., Nazıroğlu, M., Flores-Arce, M. (2012) Vitamin D supplementation modulates blood and tissue zinc, liver glutathione and blood biochemical parameters in diabetic rats fed on a zinc-deficient diet. Biol. Trace Elem. Res. 148 (3), 371-377.
[25] Kumari, D., Nair, N., Bedwal, R.S. (2011) Effect of dietary zinc deficiency on testes of Wistar rats: Morphometric and cell quantification studies. Trace Elem. in Med .Bio. 25, 47-53.
[26] Levin, G., Cogan, U., Mokady, S. (1992) Food restriction and membrane fluidity. Mech. Ageing . Dev. 62, 137-141.
[27] Ploysangam, A., Falciglia ,GA., Brehm, B.J. (1997) Effect of marginal zinc deficiency on human growth and development. Trop. Pediatr. 43, 192-197.
[28] Lee, S.L., Kwak, E.H., Kim, Y.H, Choi, J.Y., Kwon, S.T., Beattie, J.H., Kwun ,I.S.(2003) Leptin gene expression and serum leptin levels in zinc deficiency: implications for appetite regulation in rats. Med. Food. 6 (4), 281-289.
[29] Song, H.D., Hu, R.M., Peng, Y., Huang, Q. (2000) Study on the gene expression profiling in the normal human pituitary. Chin. Endocrinol. Metab. 16, 292-296.
[30] Bjursell, M., Egecioglu, E., Gerdin, A. K., Svensson , L.,Oscarsson , J., Morgan, D., Snaith, M., Törnell, J., Bohlooly, Y.M. (2005) Importance of melanin- concentrating hormone receptor for the acute effects of ghrelin. Biochem. Biophys. Res. Commun. 326, 759-765.
[31] Shay, N., Mangian, H. F. (2000) Neurobiology of zinc-influenced eating behavior. Nutr. 130, 1493-1499.
[32] Merrells, K.J., Blewett, H., Jaamieson, J.A., Taylor, C.G., Suh, M. (2009) Relationship between abnormal spermophysiology induced by dietary zinc deficiency and lipid composition in testes of growing rats. Br. Nutr. 102, 226-232.
[33] Badr, G., Bashandy, S., Ebaid, H., Mohany, M., Sayed, D. (2012) Vitamin C supplementation reconstitutes polyfunctional T cells in streptozotocin-induced diabetic rats. Eur. Nutr. 51 , 623-633.
[34] Williams, A.R., Mills, C.E., (1970) The experimental production of zinc deficiency in the rats. Brit. Nutr. 24, 989-1003.
[35] Kechrid, Z., Amamra, S., Bouzerna, N. (2007) The effect of zinc deficiency on zinc status, carbohydrate metabolism and progesterone level in pregnant rats. Turk.Med. Sci. 36, 337-342.
[36] Huber, A.M., Gershoff, S.N. (1970) Effect of dietary zinc and calcium on the retention and distribution of zinc in rats fed semi-purified diets. Nutr.100, 949-954.
[37] Kechrid, Z., Bouzerna, N., Zio M.S. (2001) Effect of low zinc diet on (65)Zn turnover in non-insulin dependent diabetic mice. Diabetes Metab. 27, 580-583.
[38] Ayinde, O.C., Ogunnowo, S., Ogedegbe, R.A. (2012) Influence of vitamin C and vitamin E on testicular zinc content and testicular toxicity in lead exposed albino rats. Pharm. Toxic. 14, 13-17.
[39] Mcardle, H.J., Andersen, H.S., Jones, H., Gambling, L. (2006) Fetal programming: causes and consequences as revealed by studies of dietary manipulation in rats. A review. Placenta. 27 (Suppl A),56-60.

[40] Jou, M.Y., Philipps, A.F., Lonnerdal, B. (2010) maternal zinc deficiency in rats affects growth and glucosemetabolism in the offspring by inducing insulin resistance postnatally. J. Nutr. 140, 1621-1627.
[41] King, J.C. (2000) Determinants of maternal zinc status during pregnancy .Amer. J. Clin. Nutr. 71,1334-1343.

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