e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(9); 821-825

Original Research Article

Serum Vitamin E Levels in the Pregnant State and in Gestational Diabetes Mellitus

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Received: 15-07-2022 / Revised: 19-08-2022 / Accepted: 13-09-2022
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Conflict of interest: Nil

Abstract

Background: In the recent years, the role of decreasing antioxidants and increasing superoxides is gaining importance as a cause of a number of medical disorders complicating pregnancy such as gestational diabetes mellitus (GDM) and pregnancy induced hypertension. Vitamin E is a naturally found antioxidant which plays an important role in the suppression of free radical-induced lipid peroxidation. The present study was undertaken to assess the levels of Vitamin E in normal pregnancy and in women with gestational diabetes mellitus.

Materials and Methods: Fifty nonpregnant controls, fifty uncomplicated pregnant and 46 women with GDM aged 20 to 35 years attending outpatient department (OPD) of Government General Hospital, Guntur, were tested for serum vitamin E levels.

Results: The mean serum vitamin E level was higher in nonpregnant women but significantly lower in women with GDM when compared to that in women with non GDM pregnancies. There is no difference in serum vitamin E levels of women with GDM who delivered macrosomic babies when compared to other GDM deliveries.

Conclusion: Serum vitamin E levels are lower in insulin resistance states like gestational diabetes mellitus.

Keywords: Gestational diabetes mellitus, Vitamin E.

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Background

Worldwide, 1 in 10 pregnancies is associated with diabetes, 90% of which are GDM. In India, one of the most populous countries globally, rates of GDM, though highly variable between 0.5-42%, are much higher than in the West [1]. Undiagnosed or inadequately treated GDM can lead to significant maternal and fetal complications.

The interaction of Advanced Glycation End Products (AGEs) and specific cellular receptors called AGE Receptors are

elevated when glucose interacts with specific amino acids on proteins. Reactive Oxygen Species oxidizes proteins that react with functional group of proteins. This causes glycation of protein which alters the cellular function and reduced capacity of antioxidant enzymes causing pancreatic beta cell dysfunction [2].

Oxidative stress may have an impact in toxemia, and there is some proof to propose that enhancement of nutrients C and E could diminish the hazard. Notwithstanding, this remaining partly doubtful, as challenged in a number of other studies [3]. We therefore intended to look into the association of serum Vitamin E levels with GDM.

Materials and methods

This is a prospective comparative study undertaken in the pregnant and nonpregnant women, aged 20 to 35 years, attending OPD at the department of Obstetrics and Gynecology at Government General Hospital, Guntur from 1st January 2019 to 1st January 2021. Women on confounding vitamin supplements or those with a history of smoking, alcohol, previous hypertension, overt diabetes, severe anemia, cardiac, pulmonary or other comorbities that could interfere with the study were excluded.

The women were divided into three groups:

Group 1- Pregnant women in 3rd trimester without complications (n=50)

Group 2- Pregnant women in 3rd trimester with confirmed gestational diabetes mellitus (n=46)

Group 3- Non pregnant healthy women as controls (n=50)

Serum Vitamin E levels were measured at Thyrocare, Mumbai by liquid chromatography- tandem mass spectrometry, as a part of a multiple test package. Water utilized for mobile phase preparations was deionized and of type 1 purity. Sample treatment reagents used were methanol (Optima™ LC/MS Grade, Fisher Scientific), ethanol (EMSURE® ACS, ISO, Reag. Ph Eur), formic acid 99% (Carlo Erba ACS - Reag. Ph.Eur. - Reag. USP.), chloroform (Carlo Erba GCMS grade ISO - ACS -Reag. Ph.Eur. - Reag. USP), and trichloroacetic acid 99% (ACS reagent). Mobile phases were 0.1% formic acid in water and 0.1% formic acid in methanol. Commercially available calibrators and controls of Recipe ClinChek® and Zivak were used. For the analysis, 100 µl of serum sample was added to 400 µl of 7:1 ethanol-chloroform mixture followed by vortex mixing and centrifugation; 50 µl of supernatant was injected into the LC-MS system. Analysis was performed on a Shimadzu Nexera X2 UHPLC autosampler coupled with an 8045 Triple quadrapole mass spectrometer (Shimadzu, Kyoto, Japan). Vitamin E was separated on a Phenomenex Kinetex C8 50mm*4.6mm chromatography column. Analytes were detected on multiple reaction monitoring mode (MRMs) and quantified based on their specific mass to charge (m/z) transitions.

Data was statistically evaluated with IBM SPSS Statistics for Windows, Version 22.0., IBM Corp., Chicago, IL.

Results:

The mean age of the normal healthy pregnant women was 25.63 ±3.38 years and in those with gestational diabetes mellitus was 26.28 ±3.23 years and was comparable.

Table 1: showing Birth Weight Distribution among Delivered Mothers (n=86)

Birth weight	Healthy pregnant mothers		GDM mothers	
	No	%	No	%
<2.5Kg	7	14	3	8.0
2.5– 3.4Kg	40	80	23	62.0
3.5– 3.9Kg	3	6	9	24.3
≥4Kg	Nil	Nil	2	5.7

The prevalence of macrosomic babies was high among GDM mothers as compared to healthy pregnant mothers, as shown in table 1.

The mean value of serum Vitamin E in non-pregnant healthy women was 1.36±0.19 mg/dl, which can be considered as the baseline reference value.

Table 2: Showing the Distribution of Serum Vitamin E Levels among the Study Participants (N=96)

Sl. No	Group	Total	Mean	SD	p value
1	Group1	50	1.46	0.14	p<0.001(1.01*10^-35)
2	Group2	46	0.89	0.13	
	Total	96	1.19	0.32	

As seen in table 2, the distribution of serum Vitamin E was significantly higher in normal healthy pregnant women (1.46 ± 0.14) compared to non-pregnant healthy females (1.36 ± 0.19), but significantly lower in GDM mothers (0.89 ± 0.13) compared to normal healthy pregnant women (1.46 ±0.14).

Among those who delivered, caesarean section was done in 62% of healthy pregnant women and 66.67% of GDM mothers. In healthy pregnant women (N=50), there were 4 patients who delivered preterm, whereas among GDM mothers (N=36), there were 4 preterm births. Out of 46 GDM cases, 36 patients had delivered, and 10 patients had not yet delivered at the time of completion of the study. Among the 36 GDM mothers who had delivered, the birth weight of baby was ≥ 3.5 kg in 10 cases of which two were macrosomic. The prevalence of macrosomic babies was high among GDM mothers as compared to healthy pregnant mothers. There is no significant difference in mean value of serum Vitamin E (p=0.21) between all GDM mothers and GDM mothers who delivered baby weighing ≥3.5kg (0.95±0.16 mg/dl) in our study.

Discussion

We had observed that levels of vitamin E in serum were significantly lower in women with GDM as compared to normal healthy pregnant women. A low level of serum vitamin E along with significant decrease in serum Glutathione peroxidase has been reported to be in favor of the overwhelming of antioxidant defense systems. Parast et al [4] have also reported similar findings as shown in the table 3.

Table 3: Showing Serum Vitamin E Comparison in Various Studies

Group	Suhail et al[5] (µmol/L)	Parast et al [4] (mg)	Present study (mg/dl)
Pregnant Healthy Controls	17.74± 2.16	16.2 ± 3.1	1.46 ± 0.14
GDM	13.21 ± 2.64	11.8 ± 3.1	0.89 ± 0.13

Studies of women with higher plasma tocopherol levels showed no such correlation between fetal and maternal plasma tocopherol concentrations between

20 and 40 weeks of gestation. However, there appear to be strong, consistent correlations between concentrations of α-tocopherol in maternal and newborn RBCs and the tendency for hemolysis in deficient states.

Johnston et al [6] in his study viewed that the initiation of vitamin supplementation varied between 8 and 22 weeks of gestation, and vitamin supplemented subjects were categorized according to whether supplementation began in week 8-12 or week 13-22. No significant differences in the various outcome measures were found between these sub-groups, indicating that the gestational point at which vitamin supplementation began did not impact on antioxidant enzyme status or lipid peroxidation markers.

The expected advantage of these antioxidant agents in 2410 ladies with a scope of clinical hazard factors has a1so been assessed in a huge multicenter randomized, treatment-controlled trial [7]. The women took nutrient C 1000 mg/day + nutrient E (RRR alpha tocopherol) 400 IU/day (n =1199) or coordinated trial (n = 1205) from the second trimester until conveyance. The rate of toxemia was comparable in the two trials (15% versus16%; RR = 0.97; 95% CI = 0.80, 1.17). All the more, low birth weight babies were born to women who took cell antioxidants than to controls (28% versus 24%; RR =1.15; CI = 1.02, 1.30), yet small size for gestational age didn't contrast between the groups (21% versus 19%; RR =1.12; CI=0.96, 1.31).

Maternal intake of foods containing vitamin E and zinc during pregnancy was associated with a reduction in the risks of developing childhood wheeze and asthma. However, vitamin E may be of potential concern when taken in the first trimester. Vitamin E intake above 14.9 mg/day in the first 8 weeks of pregnancy was associated with a 1.7-to 9-fold increased congenital heart defects (CHD)risk [8].

Moreover, Vitamin E supplementation beyond one week in premature neonates and very-low-birth-weight infants resulting in serum alpha-tocopherol concentrations more than 3.5 mg/dL has been associated with an increased risk of necrotizing enterocolitis and sepsis, due to the narrow therapeutic window [9].

Conclusion

As vitamin E levels were found to be reduced which is probably due to free radical production causing more oxidative stress in GDM mothers, preventive measures can be undertaken to all high-risk individuals and also in GDM mothers. It is possible that guarded supplementation with Vitamin E may improve the prognosis as well as may prevent the development of GDM.

The limitation of our study is the small sample size. We could also not look into the placental antioxidant levels, for better correlation, due to logistic concerns. This is only a preliminary study, and future research with large population may throw light into the possible role of such antioxidants in GDM, and the effect of supplementation on changing the course of the disorder.

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