L-Ascorbic Acid Status Of Pregnant Women And Its Potential Role In Pregnancy-Induced Stress

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Abstract

Introduction: The increased metabolic activity during pregnancy leads to an increased oxygen requirement. This in turn leads to an increased intake and utilization of oxygen resulting in elevated levels of oxidative stress via the production of reactive oxygen species.
Methods: The concentration of serum L-ascorbic acid was assayed in 90 pregnant women (age range 20-35 years) and a control group of 30 age-matched women with the aim of assessing the variation in L-ascorbic acid levels and its availability for scavenging reactive oxygen species and controlling oxidative stress during pregnancy.
Results: Serum L-ascorbate was found to generally decrease during the entire period of pregnancy. Inter-trimester mean L-ascorbic acid concentrations in serum were all lower than the control serum L-ascorbic acid concentration. The lowest serum concentration of L-ascorbic acid was found in the first trimester, 1.10 ± 0.01 mg/dl, $p < 0.05$ relative to the control serum L-ascorbic acid concentration of 3.05 ± 0.13 mg/dl. Within trimester L-ascorbate was lowest in the 1-2 months of pregnancy, 0.84 ± 0.01 mg/dl vs. 3.05 ± 0.13 mg/dl (control), $p < 0.05$.
Conclusion: These results indicate a compromised ability to scavenge reactive oxygen species, significant perturbation of other L-ascorbate-requiring metabolic/physiological activities during pregnancy and the need for vitamin C supplementation for pregnant women.

INTRODUCTION

Many free radicals are produced in the body as a result of the myriad of biochemical processes taking place in normal metabolism [1]. Oxygen-derived free radical s account for 95 % of such radicals [2]. These free radicals perform some physiologic function to some degree in the body such as, participating in xenobiotics metabolism, biosynthesis and clearance of microorganisms [3,4,5]. The normal homeostasis of these free radicals is maintained by anti-oxidants and anti-oxidases, leading to a dynamic balance between production and clearance [6]. An imbalance between reactive oxygen species and anti-oxidant defense mechanisms of a cell leads to an excessive production of oxygen metabolites, creating a condition known as ‘oxidative stress' [7]. Such free radicals can attack polyunsaturated fatty acids of membranes, leading to lipid peroxidation and disruption of intracellular calcium homeostasis and consequent cellular apoptosis [8]. Free radicals can also destroy key intracellular enzymes, including free radical scavenger enzymes, disrupt DNA replication and initiate the process of carcinogenesis [9,10].

Free radical-induced oxidative injury have been reported to have a role in the pathogenesis of a number of diseases, including cancer, atherosclerosis, diabetes mellitus, epilepsy, radiation damage, cellular aging, reperfusion damage, inflammatory diseases and Parkinsonism [2, 10,11,12,13,14,15]. Free radical defenses in the body consist of a complex anti-oxidant system comprising of vitamins A, C, E, glutathione and anti-oxidant enzymes [16,17]. These enzymes include glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase [16]. Pregnancy is a developmental crisis in a woman's life. It places a great demand on her body and requires adaptation. Changes in many of the body's biochemical function during pregnancy leads to a high demand for energy and an increased oxygen requirement [18]. This leads to intake and utilization of oxygen, resulting in increased levels of oxidative stress and the consequent acceleration in the production of reactive oxygen species [19]. In this study, the serum concentration of L-ascorbic acid which makes up over 80% of the vitamin C activity was assessed in pregnant women in three different trimesters of pregnancy with the aim of determining the effect of pregnancy on serum L-ascorbic acid concentration and its availability for the scavenging of reactive oxygen species produced as a result of pregnancy-induced oxidative stress.

SUBJECTS AND METHODS

Subjects. The subjects enrolled in this study comprised of 90 pregnant women (30 in each trimester) within the age range of 20-35 years. 30 age and sex-matched non-pregnant adult females were also enrolled for comparative studies. None of the study or control subjects had taken any form of vitamin C supplementation within a period of two weeks prior to participation in the study.

Assay for serum vitamin C. Serum L-ascorbic acid was assayed using the 2, 6-dichlorophenolindophenol method [20].

Ethics. The study was conducted in compliance with the Lisbon Declaration on the Rights of the Patient [21].

Data analysis. Data are presented as mean ± SEM. Data analysis was done using the Minitab-10 Statistical Software. Mean serum L-ascorbic acid concentration within and between trimesters were compared using One-Way ANOVA. The method of Least Significant Difference (LSD) was used to assess for significant differences between means where the ANOVA results returns a p value < 0.05. p values < 0.05 were considered significant.

RESULTS

Figure 1

Table 1: Serum L-ascorbic acid concentration within first trimester (mg/dl).

Age of pregnancy	Mean ± SEM
1-2 months	0.84 ± 0.01^{*a}
3 months	1.17 ± 0.09^{*a}
Control	3.05 ± 0.13*

* Differences significant at $p < 0.05$. (One Way ANOVA)
^{a} Differences not significant at $p < 0.05$ (LSD)

Figure 2

Table 2: Serum L-ascorbic acid concentration within second trimester (mg/dl).

Age of pregnancy	Mean ± SEM
4 months	2.44 ± 0.35^{*a}
5 months	2.75 ± 0.27^{*a}
6 months	2.23 ± 0.16^{*a}
Control	3.05 ± 0.13*

* Differences significant at $p < 0.05$. ((One Way ANOVA)
^{a} Differences not significant at $p < 0.05$ (LSD)

Figure 3

Table 3: Serum L-ascorbic acid concentration within third trimester (mg/dl).

Age of pregnancy	Mean ± SEM
7 months	1.70 ± 0.12^{*a}
8 months	1.30 ± 0.05^{*b}
9 months	1.70 ± 0.06^{*a}
Control	3.05 ± 0.13*

* Differences significant at $p < 0.05$. (One Way ANOVA)
^{ab} Differences significant at $p < 0.05$ (LSD)

Figure 4

Table 4: Inter trimester variation in mean serum L-ascorbic acid concentration (mg/dl).

Age of pregnancy	Mean ± SEM
1st trimester	1.10 ± 0.09^{*a}
2nd trimester	2.42 ± 0.13^{*b}
3rd trimester	1.61 ± 0.09^{*a}
Control	3.05 ± 0.13*

* Differences significant at $p < 0.05$. (One Way ANOVA)
^{ab} Differences significant at $p < 0.05$ (LSD)

The results obtained are shown in tables 1-4. Within the first trimester, serum L-ascorbic acid concentration is lowest in the 1 – 2 months of pregnancy. The mean serum L-ascorbic acid in this period was found to be 0.84 ± 0.01 mg/dl. It is significantly lower than the mean serum L-ascorbic acid concentration in the third month of pregnancy. Compared to the serum L-ascorbic acid in the controls, the serum L-ascorbic acid concentration within the first trimester of pregnancy is significantly lower, p < 0.05, table 1. The second trimester L-ascorbic acid concentrations in serum are higher than the mean L-ascorbic acid concentration obtained in the first trimester. The peak L-ascorbic acid concentration within this trimester was obtained in the fifth month of pregnancy as shown in table 2. The mean L-ascorbic acid concentrations within the second trimester are all however lower than the control serum L-ascorbic acid concentration of 3.05 ± 0.13 mg/dl, $p < 0.05$. The L-ascorbic acid concentrations within the last three months of the third trimester are within the same range except for the 8th month where a value of 1.30 ± 0.06 mg/dl was obtained, table 3. The control value of 3.05 ± 0.13 mg/dl is significantly higher than all the mean L-ascorbic acid concentrations within the last three months of pregnancy, $p < 0.05$. The inter-trimester comparison of the mean L-ascorbic acid concentrations shows a peak L-ascorbic acid value of 2.42 ± 0.13 mg/dl in the second trimester. This is significantly higher than the mean values for both first and third trimesters. The values are all lower than the control L-ascorbic acid concentration as shown in table 4, $p < 0.05$.

DISCUSSION

There is a significant reduction in the serum L-ascorbic acid concentration throughout the period of pregnancy with the highest decrease in the first trimester. As reported by Renata et al.[19] changes in the physiological state during pregnancy necessitates an increase oxygen intake and utilization. This leads to an increased level of oxidative stress. The increased utilization of L-ascorbic acid to neutralize the toxicity of the resulting reactive oxygen species consequent to increased oxidative stress can account for the low serum concentration of this vitamin. L-ascorbic acid is also involved in maintaining the tocopherol cycle, necessary for the peroxyl radical scavenging action of vitamin E in the biological lipid phase [22]. Low serum L-ascorbic acid can therefore lead to a compromised defense against free radical-induced lipid peroxidation. Lipid peroxidation is known to be potentially harmful because its uncontrolled, self-enhancing process causes disruption of membranes, lipids and other cell components [23]. The simultaneous decrease in L-ascorbic acid and the accompanying ineffectual vitamin E free radical scavenger function can cause damage to cellular organelles and lead to oxidative stress during pregnancy with undesirable effects on fetal development and maternal health. Considering the catalytic role of ascorbic acid in enhancing iron absorption [24,25] the low serum ascorbate can lead to a decrease in the absorption and subsequent utilization of iron which is required for the proper maintenance of pregnancy and fetal growth. In addition, during pregnancy resistance to infection is generally decreased. Similarly fetal and neonatal immunity is low. Low serum L-ascorbic acid will further complicate this delicate immune status since L-ascorbic acid is known to play a significant role in boosting immunity [26,27]. Since earlier reports have confirmed the importance of vitamin C in safe delivery and the prevention of premature abortions [28,29] we conclude from these results that pregnant women should be placed on daily supplemental doses of vitamin C to boost maternal antioxidant defenses and help improve maternal and fetal immune status.

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