# Ascorbic acid intake during pregnancy

**Kristina Podolska[1], Dana Mazankova[1], Maria Goboova[2], Ivan Vano[2]**

The continuing global increase in allergic conditions and diseases in children is now a serious public health and scientific issue. Amongst other concerns is the maternal antenatal diet as intake of essential nutrients. Even small deficits in essential vitamin C can permanently impair the developing brain for example. In this article, we first review ascorbic acid deficiency in different organs of both mother and foetus. However, major emphasis is on the importance of vitamin C in foetal immunity with studies showing an inverse relationship between maternal intake of fresh fruit and vegetables and allergic conditions in childhood, *inter alia*. Other review results are included.

**Key words:** pregnancy, ascorbic acid, ascorbic acid deficiency, foetal health

Received: July 4, 2023; Revised: August 28, 2023; Accepted: August 28, 2023; Available online: September 6, 2023
https://doi.org/10.5507/bp.2023.035


[1]*Department of Applied Pharmacy, Faculty of Pharmacy, Masaryk University, 612 00 Brno, Czech Republic*
[2]*Department of Internal Medicine, Teaching Hospital Nitra, 949 01 Nitra, Slovak Republic*
*Corresponding author: Dana Mazankova, e-mail: mazankovad@pharm.muni.cz*

## INTRODUCTION

Ascorbic acid is a vitamin well-known as vitamin C. Other chemical names such as ascorbate or antiscorbutic vitamin are also used. Vitamin C is the generic name for l-ascorbic acid, the chemical formula is C6H8O6 and its structure is analogous to that of glucose[1]. It is a white or very pale-yellow powder, almost odorless, highly soluble in water, but insoluble in ether, chloroform, benzene, petroleum ether, oils, fats and fat solvents[2]. Its derivates include sodium l-ascorbate (sodium ascorbate), calcium l-ascorbate (calcium ascorbate), zinc-ascorbate, 6-palmityl-l-ascorbic acid (ascorbyl palmitate) (ref.[1]). These provide a broader and more useful spectrum of positive properties for the human body[3]. Vitamin C is absorbed predominantly in the small intestine[4], as well as in the buccal mucosa and stomach[1]. Intestinal absorption is dose dependent[5].

Ascorbic acid is used to prevent scurvy, it is also used as an antioxidant, to improve wound and bone healing and, as an effective antiviral agent[2].

According to some reports, around 5% to 10% (ref.[6]) of adults in the west, have ascorbic acid deficiency. This information can indicate that pregnant women will have a similar likelihood of ascorbic acid deficiency or even higher due to altered nutritional requirements[6].

## MATERIALS AND METHODS

This review covers the published literature on ascorbic acid intake during pregnancy. Key articles were retrieved mainly from PubMed database. Only articles written in English were included. There were no exclusion criteria. Scientific publications covering the period from 1986 to 2023 were included. The search strategy used the terms: "ascorbic acid deficiency in pregnancy," "vitamin C deficiency in pregnancy," "ascorbic acid and pregnancy," "vitamin C and pregnancy," "ascorbic acid deficiency," "ascorbic acid and foetus," "foetal deficiency of vitamin C," "foetus and ascorbic acid," "foetus and vitamin C," "foetal health and vitamin C," "ascorbic acid and the immune system in pregnancy," "ascorbic acid and folic acid in pregnancy" and other term-related versions with focus on foetal health and ascorbic acid importance during foetal development.

## RESULTS

### Various consequences of ascorbic acid deficiency during pregnancy on maternal and foetal health

There are various consequences of ascorbic acid deficiency during pregnancy. In order to simplify the picture of the severity of ascorbic acid deficiency, the following Table 1 was created in three sections. Firstly, maternal organ systems, secondly, the maternal-foetal unit, a structurally and functionally coherent metabolic unit shared by mother and foetus, and thirdly, foetal organ systems.

To underlie the influence of ascorbic acid deficiency and for better orientation in the table, the following abbreviations were used:

IND stands for Indirect Association of Ascorbic Acid Deficiency in maternal organ systems increasing the risk for other diseases. This abbreviation is used, when a lower maternal serum concentration of ascorbic acid is present, and although the deficiency doesn't have severe direct impact on pregnancy, it may indirectly increase risk for diseases during pregnancy for the mother and foetus and therefore subsequently affect pregnancy outcomes.

IND means that maternal ascorbic acid deficiency should not directly lead to a harm in foetal and maternal health, due to presence of next barrier protective mechanisms or other back-up mechanisms of mother or foetus.

DIR stands for Direct Association of Ascorbic Acid Deficiency in maternal and foetal body systems increasing the risk or posing a risk for adverse foetal outcomes and also there is present foetal ascorbic acid deficiency for foetal normative requirements. DIR means that maternal ascorbic acid deficiency may directly with higher degrees of severity jeopardize foetal health mainly by direct but also by possible consecutive manner, but it may also affect maternal health with higher degrees of severity, if the condition is untreated.

In general, there is a lack of information specifically related to vitamins deficiencies, including ascorbic acid, during pregnancy, and its impact on maternal and foetal health. For this reason, sometimes data derived from ascorbic acid deficiency in adults including men and non-pregnant patients are applied to pregnant women.

The following diseases presented in the table do not represent all possible clinical cases resulting from ascorbic acid deficiency. The table was compiled to provide an overview resulting from maternal ascorbic acid deficiency and its impact on maternal and foetal health, and to emphasize the biological and functional importance of ascorbic acid in the human body. In brackets are shown studies from which the given information originated.

**Table 1.** Potential risk or adverse effects of ascorbic acid deficiency for maternal and foetal health during the pregnancy.

| Maternal body systems | Effect of ascorbic acid deficiency on maternal systems | Increased risk for given disease for mother and foetus | Ref. |
|---|---|---|---|
| Circulatory and cardio-vascular system | DIR | Gestational hypertension (human studies – prospective study) | 7 |
| | DIR | Decrease in capillary strength (theoretical source – review) | 8 |
| Gastrointestinal and excretory system | IND | Affect composition in gut microbes (human studies – pilot study) | 9 |
| | DIR | Worsen absorption of iron (theoretical source – review) | 10 |
| Endocrine system | DIR | Gestational diabetes (human studies – prospective study) | 7 |
| Exocrine or integumentary system | IND | Impaired barrier integrity and wound healing (theoretical source – review) | 11 |
| Immune and lymphatic system | DIR | Impaired modulation of immune defense (theoretical source – review) | 11 |
| Muscular system | DIR | Worsen skeletal muscle functions due to long-term deficiency (animal studies) | 12 |
| Nervous system | DIR | Altered neuronal maturation with impact on neurotransmitters activity (theoretical source – review) | 13 |
| Renal and urinary system | | Insufficient data | |
| Reproductive system | DIR | Premature rupture of placental membranes (controversial) (human studies – prospective study) and (in vivo and in vitro studies) | 7,14 |
| | DIR | Premature birth (controversial) (human studies – prospective study) and (theoretical source-review) | 7,15 |
| | DIR | Infertility (controversial) (human studies – a cross-sectional study) and (human studies – prospective randomized double-blind study) | 16,17 |
| | DIR | Stillbirths (controversial) (human studies – a cross-sectional study) and (human studies – randomized placebo controlled clinical trial) | 16,18 |
| | DIR | Increased probability of abortion (controversial) (human studies – a cross-sectional study) and (human studies – randomised or quasi-randomised controlled trials) | 16,19 |
| Respiratory system | IND | Can be increased incidence of pneumonia and worsen respiratory symptoms (theoretical source – academic dissertation) (concretely specificized) | 20 |
| Skeletal system | IND | Impaired bone health (theoretical source – review) | 21 |
| Uncategorized | DIR | Scurvy (theoretical source – book) | 22 |
| **Maternal-foetal unit** | DIR | Foetal, uterine, and placental hemorrhages (human studies – a cross-sectional study) | 16 |
| | DIR | Insufficient attachment of the placenta to the uterus (human studies – a cross-sectional study) | 16 |

**Table 1.** Potential risk or adverse effects of ascorbic acid deficiency for maternal and foetal health during the pregnancy. *(Continued)*

| Foetal body systems | Effect of ascorbic acid deficiency on foetal systems | Consequences on foetal side | |
|---|---|---|---|
| Circulatory and cardio-vascular system | DIR | Chronic prenatal hypoxia can be worsened (animal studies – longitudinal study) concretely specified) | 23 |
| Gastrointestinal and excretory system | | Insufficient data | |
| Endocrine system | DIR | Intrauterine growth retardation (controversial) (human studies – prospective study) and (human studies – randomised or quasi-randomised controlled trials) | 7,19 |
| Exocrine or integumentary system | | Insufficient data | |
| Immune and lymphatic system | | Insufficient data | |
| Muscular system | | Insufficient data | |
| Nervous system | DIR | Complications of CNS development (human studies – a cross-sectional study) | 16 |
| Renal and urinary system | | Insufficient data | |
| Reproductive system | | Insufficient data | |
| Respiratory system | DIR | May adversely affect lung maturation (animal studies) | 24 |
| Skeletal system | DIR | Worsen foetal bone development (human studies – a cross-sectional study) | 16 |
| | DIR | Impaired collagen synthesis (theoretical source – book) | 22 |

Human studies – the information is based on the study, which used human data in their methodology; animal studies – the information is based on the study, which used animal data in their methodology; theoretical source – the information is based on theoretical description, review, book or research; concretely specificized – the information applies to a specific case and disease; in vivo and in vitro studies – the information is based on combination of in vivo and vitro studies; controversial – there are studies which confirm the beneficial role of ascorbic acid and at the same time there are studies which disprove beneficial role of ascorbic acid on given disease, circumstance or condition, insufficient data – there are no detailed data, which could provide sufficient information.
DIR, Direct Association of Ascorbic Acid Deficiency – deficiency can represent direct harm, maternal and foetal health can be jeopardized with higher degree of severity if the appropriate treatment is not initiated on time; IND, Indirect Association of Ascorbic Acid Deficiency – deficiency does not represent direct harm, but can indirectly increase risk for negative maternal and foetal outcomes.

**Characteristics of ascorbic acid intake during pregnancy**

Vitamin C (ascorbic acid) is a water-soluble vitamin and the daily recommended allowed intake in pregnant women is 85 mg/day (ref.[25]). Absorption and elimination are dose-dependent[26]. A related issue is whether there is a difference in the bioavailability of ascorbic acid when the mother consumes it as fruit and vegetables or as synthetic ascorbic acid. Carr et al. (2013) carried out a study in men who consumed kiwi-fruit and they found no difference in the bioavailability of kiwi-fruit-derived vitamin C in comparison to chewable vitamin C of equivalent dosage, however, the micronutrients and phytochemicals in kiwi-fruit could have added health benefits[27]. We assume that a similar situation applies to pregnant women although during pregnancy other factors are present which influence drug absorption and bioavailability.

Contraindication to the use of ascorbic acid in pregnant women is similar to adults with thalassemia, G6PD deficiency (Glucose-6-phosphate dehydrogenase deficiency) (ref.[4]), sickle cell anaemia, and hemochromatosis, before and during angioplasty. Patients with diabetes mellitus and renal impairment should be cautious[4].

There is less data about ascorbic acid overdose in pregnant women. The available information is based on animal data, some clinical studies and observations in adult patients. For example, maternal ascorbic acid overdosage can increase the risk of hyperoxaluria[28]. High dosing can also lead to nausea, abdominal pain and other gastrointestinal problems. High doses can increase alanine aminotransferase (ALT) (ref.[29]) with short-term toxic effects on the liver[29]. As regards the foetus, long-term antenatal overdosing can cause scurvy later in the infant's life[30].

**Ascorbic acid importance for mother and foetal outcomes**

Ascorbic acid can reduce the risk of maternal anaemia[19]. However, ascorbic acid intake had no impact on preventing preterm birth[15].There is also no convincing evidence that ascorbic acid has a predominantly beneficial role in lowering the risk for pre-eclampsia and poor foetal growth[18,19]. A maternal diet which includes consumption of fruits and vegetable with sufficient amount of ascorbic acid is related to increased foetal growth in mid-pregancy[31]. However, Rumbold et al. (2015), concluded that the data do not support the theory that routine vitamin C supplementation alone or in combination with other supplements can prevent poor foetal growth[19]. Richter et al. (2012), observed a relationship between ascorbic acid supplementation in pregnant rats with and without induced maternal hypoxia. Ascorbic acid was put into drinking water, and cases with and without added ascorbic acid were observed. Pregnant rats were subjected to normoxic pregnancy or 13% (ref.[32]) oxygen chronic hypoxia. Maternal hypoxia increased oxidative stress which could be prevented by administration of ascorbic acid which also improved placental function and protected foetal growth in pregnancy complicated by foetal hypoxia. There are, however, differences between ascorbic acid metabolism in rats and humans. Rats synthetize their own ascorbic acid[32].

Preterm and premature rupture of the membranes is a pregnancy complication when the membrane rupture happens before 37 weeks of gestation, hence it is called preterm. The abbreviation PROM (premature rupture of membranes) (ref. [33]) or PPROM (preterm rupture of membranes) (ref.[33]) is used for preterm rupture of membranes[33]. Mercer et al. (2010) observed that low ascorbic acid intake before or during pregnancy also leads to increased risk of preterm PROM and that supplementation with anti-oxidant vitamins may be effective in preventing it. One study reported that daily supplementation with ascorbic acid after the 20th week of gestation reduced the incidence of PROM (ref.[14]). However, another study found that ascorbic acid was ineffective in the management or prevention of PPROM (ref.[7]).

Coker et al. (2022), discussed nutriepigenomics and neurodevelopment, providing new information on the importance of ascorbic acid in neurodevelopmental epigenetics. Ascorbic acid appears to have a role in neurodevelopment and has neurogenic-positive effects through epigenetic interactions with deoxyribonucleic acid (DNA) (ref.[34]) at the intracellular level. The authors write that, in recent years, a number of epigenetic enzymes that are active during embryonic development have been found to require vitamin C as a cofactor[34].

The relation between ascorbic acid and fertility is that ascorbic acid as antioxidant can improve the female menstrual cycle and ovulation[35]. Antioxidant supplementation can reduce female infertility associated with oxidative stress[36].

Ascorbic acid may affect fertility, because vitamin C positively influences ovarian function. Based on the authors' research, ascorbic acid excretion is increased and declines right before ovulation, and then excretion promptly increase again in post-ovulation. It is possible that ascorbic acid levels may affect the process of ovulation. Ascorbic acid levels have been also found in high concentrations in the corpus luteum[37].

IVF (ref.[38]) is a form of assisted reproductive technology[38]. According to one study ascorbic acid administration during hormonal stimulation had statistically insignificant impact in terms of a higher number of pregnancies. But it has been observed that ascorbic acid is able to increase the number of pregnancies in a non-smoker group of women[39]. The influence of ascorbic acid in the luteal phase during infertility treatment, showed no beneficial impact of ascorbic acid on IVF-ET (in vitro fertilization and embryo transfer) (ref.[17]).

Another study showed that the maternal diet is associated with diseases that can develop later in life. There was an observed connection- if the foetus has insufficient access to ascorbic acid from the mother´s diet during its development, it can lower the infant’s fertility in the future[40].

As in the majority of adults, side effects may occur in pregnant women. The side effects of ascorbic acid are caused in most cases by a large single dose or large single doses administered repeatedly, while another factor, which can exacerbate the side effects, is renal insufficiency, and large doses of ascorbic acid may increase the absorption of heavy metals. Repeated large single doses may lead to gastrointestinal complications such as – diarrhoea, abdominal pain. In the oral cavity, it can cause enamel erosion. As regards the renal system, renal stones or oxalate salts[1] may occur.

Description of the antioxidant activity of ascorbic acid is comprehensive. To sum up, ascorbic acid protects the cells from free radical damage[41]. Ascorbic acid, Vitamin E and Coenzyme Q cooperate in a sequence of interaction. Ascorbic acid scavenges free radicals in the aqueous phase[41,42].

**Ascorbic acid and stimulation of maternal and foetal immune system**

Ascorbic acid supports the immune activity of both innate and adaptive immune systems. It has the ability to sequester phagocytes, increase chemotaxis, and is involved in the proliferation of B- and T-cells[11]. West et al. (2012) report that sufficient maternal ascorbic levels have impact on foetal immunity and foetal programming[43].

Apropos immunity, West et al tested whether antioxidant intakes in pregnancy influence foetal immune programming and the risk of allergic disease. They selected the antioxidants β-carotene, vitamin C, vitamin E, copper and zinc, and their relationship with infant allergic outcomes. The main relationships with allergic outcomes were found with dietary vitamin C and copper. Specifically, higher maternal dietary vitamin C intake was associated with a reduced risk of any diagnosed infant allergic disease and wheeze. There was an inverse linear relationship between vitamin C and food allergy[43].

Ascorbic acid in the form of intracellular ascorbate is present in the maternal lymphocytes, monocytes and neutrophils. There is scientific evidence that during inflammation, plasma and cellular ascorbate levels are lowered. The ability of ascorbate can be influenced by ascorbate-dependent enzymes[44]. This may be applied to pregnant women and may influence the maternal immune function.

During pregnancy, ascorbic acid levels can affect migration of neutrophils and, may affect phagocyte cells and Natural killer (NK) cells[45].

**Possible effect of ascorbic acid on foetal lung maturation**

McGillick et al. (2021) described the effect of ascorbic acid on foetal lung maturation in sheep. The sheep had been administered ascorbic acid intravenously for one month in late gestation. The study found that ascorbic acid administration had impact on the expression of genes regulating antioxidant defence therefore influencing lung development and, the foetal lung gene expression was increased. Surfactant maturation was also increased.

However, no effect on the expression of protein markers on surfactant-protein producing cells was observed[24].

**Folic acid and ascorbic acid influence foetal health**

Habibzadeh et al. (1986), described severe consequences of folic acid and ascorbic acid deficiency. Both of these vitamins are indispensable in foetal physiological development. Consequences resulting from changes of folic acid and ascorbic acid dosage in female guinea-pigs have been observed. To sum it up, reproductive changes were observed in animal species during organogenesis after folic acid and ascorbic acid content in the diet was changed. Deficiency of these vitamins during dietary restriction led to malformations in animal foetuses[46].

## CONCLUSION

It can be concluded that ascorbic acid is linked to the health of both mother and foetus, and it is involved in most body processes and organ systems. During pregnancy, ascorbic acid has the ability to enhance the reparation processes of damaged maternal epithelial tissue and, it influences the maternal and foetal bone health. It has been found to be a potent antiviral agent, it is known to be an effective antioxidant, and it plays a significant role in immunity. Ascorbic acid daily recommended allowed intake in pregnant women is 85 mg/day. Appropriate and optimized intake of ascorbic acid in pregnancy mainly reduces the risk for maternal anaemia, but results on the prevention of pre-eclampsia remain inconclusive. Deficiency of ascorbic acid in pregnancy on the maternal side can lead to a wide spectrum of abnormalities and diseases. Ascorbic acid deficiency in the maternal-foetal unit is shown, for example, by foetal, uterine, and placental haemorrhages and insufficient attachment of the placenta to the uterus.

**Search strategy and selection criteria**

Our research strategy was aimed for including studies, which explained importance of ascorbic acid in the pregnancy with effect on maternal and foetal health. We have tried to include as many human data as possible, but in certain cases there were present only data of non-pregnant patients, general population, animal data, in vitro and in vivo studies or solely theoretical sources. Scientific publications covering the period from 1986 to 2023 were included. We have used different approaches to be able to provide different views on maternal ascorbic acid deficiencies and foetal ascorbic acid deficiencies. The search strategy used primary terms as: "ascorbic acid and pregnancy," "ascorbic acid and foetus," "ascorbic acid deficiency in pregnancy" and other term-related versions.

**Acknowledgement:** I am grateful to co-authors with whom I have had the opportunity to work during the elaboration of this review article.

**Authors contributions:** KP: originated the idea for this manuscript, literature review, writing – original draft, final adjustments of manuscript, visualization; DM: conceived the review article design and created conception for manuscript, final adjustments of manuscript, supervision; MG: provided an approval, expert opinion, final adjustments and professional consultations; IV: provided approval, final adjustments of manuscript, supervision.

**Conflict of interest statement:** None declared.

## REFERENCES

1. Yussif NM. Vitamin C. Jean Guy LeBlanc. Vitamin C - an Update on Current Uses and Functions. London: Intechopen 2018. doi: 10.5772/intechopen.81783
2. PubChem: Ascorbic acid. [cited 2023-02-03] Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Ascorbic-Acid
3. Macan AM, Kraljević TG, Raić-Malić S. Therapeutic Perspective of Vitamin C and Its Derivates. Antioxidants (Basel) 2019;8(8):247. doi:10.3390/antiox8080247
4. StatPearls Publishing LLC. Vitamin C (Ascorbic Acid). 2022. [cited 2023-02-03] Available from: https://www.ncbi.nlm.nih.gov/books/NBK499877/
5. National Academies Press (US): Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. 2000. [cited 2023-03-08] Available from: https://www.ncbi.nlm.nih.gov/books/NBK225480/
6. Lindblad M, Tveden-Nyborg P, Lykkesfeldt J. Regulation of Vitamin C Homeostasis during Deficiency. Nutrients 2013;5(8):2860-79. doi: https://doi.org/10.3390/nu5082860
7. Ugwa EA, Iwasam EA, Nwali MI. Low Serum Vitamin C Status Among Pregnant Women Attending Antenatal Care at General Hospital Dawakin Kudu, Northwest Nigeria. Int J Prev Med 2016;7:40. doi: 10.4103/2008-7802.176166
8. Vitagliano T, Garieri P, Lascala L, Ferro Y, Doldo P, Pujia R, Pujia A, Montalcini T, Greco M, Mazza E. Preparing Patients for Cosmetic Surgery and Aesthetic Procedures: Ensuring an Optimal Nutritional Status for Successful Results. Nutrients 2023;15(2):352. 10.3390/nu15020352
9. Otten AT, Bourgonje AR, Peters V, Alizadeh BZ, Dijkstra G, Harmsen HJM. Vitamin C Supplementation in Healthy Individuals Leads to Shifts of Bacterial Populations in the Gut. A Pilot Study. Antioxidants (Basel) 2021;10(8):1278. doi: 10.3390/antiox10081278
10. Piskin E, Cianciosi D, Gulec S, Tomas M, Capanoglu E. Iron Absorption: Factors, Limitations, and Improvement Methods. ACS Omega 2022;7(24):20441-56. doi: 10.1021/acsomega.2c01833
11. Carr AC, Maggini S. Vitamin C and Immune Function.Nutrients 2017;9(11):1211. doi: 10.3390/nu9111211
12. Takisawa S, Takino Y, Lee J, Machida S, Ishigami, A. Vitamin C Is Essential for the Maintenance of Skeletal Muscle Functions. Biology (Basel) 2022;11(7):955. doi: https://doi.org/10.3390/biology11070955
13. Kocot J, Luchowska-Kocot D, Kiełczykowska M, Musik I, Kurzepa J. Does Vitamin C Influence Neurodegenerative Diseases and Psychiatric Disorders? Nutrients 2017;9(7):659. doi: 10.3390/nu9070659
14. Mercer BM, Abdelrahim A, Moore RM, Novak J, Kumar D, Mansour JM, Perez-Fournier M, Milluzzi CJ, Moore JJ. The impact of Vitamin C supplementation in pregnancy and in-vitro upon fetal membrane strength and remodeling. Reprod Sci 2010;17(7):685-95. doi: 10.1177/1933719110368870
15. Thorp J, Allen I. Vitamin C Supplementation in Pregnancy – Does it Decrease Rates of Pre-term Birth: A Systematic Review. Am J Perinatol 2014;31(2):91-8. doi:10.1055/s-0033-1338171
16. Juhl B, Lauszus FF, Lykkesfeldt J. Poor Vitamin C Status Late in Pregnancy Is Associated with Increased Risk of Complications in Type 1 Diabetic Women: A Cross-Sectional Study. Nutrients 2017;9(3):186. doi: 10.3390/nu9030186
17. Griesinger G, Franke K, Kinast C, Kutzelnigg A, Riedinger S, Kulin S, Kaali SG, Feichtinger W. Ascorbic Acid Supplement During Luteal Phase in IVF. J Assist Reprod Genet 2002;19(4):164-8. doi: 10.1023/A:1014837811353
18. Kiondo P, Wamuyu-Maina G, Wandabwa J, Bimenya GS, Tumwesigye NM, Okong P. The effects of vitamin C supplementation on pre-eclampsia in Mulago Hospital, Kampala, Uganda: a randomized pla-

cebo controlled clinical trial. BMC Pregnancy Childbirth 2014;14:283. doi: 10.1186/1471-2393-14-283
19. Rumbold A, Ota E, Nagata CH, Shahrook S, Crowther CA. Vitamin C supplementation in pregnancy. Cochrane Database Syst Rev 2015;2015(9):CD004072. doi: 10.1002/14651858.CD004072.pub3
20. Hemilä H. Do vitamins C and E affect respiratory infections? Academic dissertation. 2006 January, Helsinky, Finland; p 50-60.
21. Chin K-Y, Ima-Nirwana S. Vitamin C and Bone Health: Evidence from Cell, Animal and Human Studies. Curr Drug Targets 2018;19(5):439-50. doi: 10.2174/1389450116666150907100838
22. Tripathy SN. Nutrition and Pregnancy ECAB. New Delhi: Elsevier India; 2014. p 17.
23. Giussani DA, Camm EJ, Niu Y, Richter HG, Blanco CE, Gottschalk R, Blake EZ, Horder KA, Thakor AS, Hansell JA, Kane AD, Wooding FBP, Cross ChM, Herrera EA. Developmental Programming of Cardiovascular Dysfunction by Prenatal Hypoxia and Oxidative Stress. Plos One 2012;7(2):e31017. doi: 10.1371/journal.pone.0031017
24. McGillick EV, Orgeig S, Allison BJ, Brain KL, Niu Y, Itani N, Skeffington KL, Kane AD, Herrera EA, Morrison JL, Giussani DA. Molecular regulation of lung maturation in near-term fetal sheep by maternal daily vitamin C treatment in late gestation. Pediatr Res 2022;91:828-38. doi: 10.1038/s41390-021-01489-4
25. Kominiarek MA, Nutrition Recommendations in Pregnancy and Lactation. Med Clin North Am 2016;100(6):1199-1215. doi: 10.1016/j.mcna.2016.06.004
26. Lykkesfeldt J, Tveden-Nyborg P. The Pharmacokinetics of Vitamin C. Nutrients 2019;11(10):2412. doi:10.3390/nu11102412
27. Carr AC, Bozonet SM, Pullar JM, Simcock JW, Vissers MCM. A Randomized Steady-State Bioavailability Study of Synthetic *versus* Natural (Kiwifruit-Derived) Vitamin C. Nutrients 2013;5(9):3684-95. doi: 10.3390/nu5093684
28. Hans U, Edward B. Regular vitamin C supplementation during pregnancy reduces hospitalization: outcomes of a Ugandan rural cohort study. Pan Afr Med J 2010;5:15. doi: 10.4314/pamj.v5i1.56178
29. National Institute of Diabetes and Digestive and Kidney Diseases: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury 2012. [cited 2023 March 9] Available from: https://www.ncbi.nlm.nih.gov/books/NBK548448/
30. World Health Organization: Scurvy and its prevention and control in major emergencies.1999. Available from: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwig7cvI8IT8AhWY8rsIHUqUB2gQFnoECAsQAQ&url=https%3A%2F%2Fwww.unhcr.org%2F4cbef0599.pdf&usg=AOvVaw0lzJ-J4ZszzNzoad7O-hjZ
31. Jang W, Kim H, Bo-Eun Lee BE, Chang N. Maternal fruit and vegetable or vitamin C consumption during pregnancy is associated with fetal growth and infant growth up to 6 months: results from the Korean Mothers and Children's Environmental Health (MOCEH) cohort study. Nutr J 2018;17(1):105. doi: 10.1186/s12937-018-0410-6.
32. Richter HG, Camm EJ, Modi BN, Naeem F, Cross CM, Cindrova-Davies T, Spasic-Boskovic O, Dunster C, Mudway IS, Kelly FJ, Burton GJ, L Poston L, Giussani DA. Ascorbate prevents placental oxidative stress and enhances birth weight in hypoxic pregnancy in rats. J Physiol 2012;590(6):1377-87. doi: 10.1113/jphysiol.2011.226340.
33. Dayal S, Hong PL. Premature Rupture Of Membranes. 2022. [cited 2023 March 9] Available from: https://www.ncbi.nlm.nih.gov/books/NBK532888/
34. Coker SJ, Smith-Díaz CC, Dyson RM, Vissers MCM, Berry MJ. The Epigenetic Role of Vitamin C in Neurodevelopment. Int J Mol Sci 2022;23(3):1208. doi: 10.3390/ijms23031208
35. Progyny: The Best Vitamins and Supplements to Boost Your Fertility. Available from: https://progyny.com/education/the-best-vitamins-and-supplements-to-boost-your-fertility/
36. Tesarik J. Towards Personalized Antioxidant Use in Female Infertility: Need for More Molecular and Clinical Studies. Biomedicines 2021;9(12):1933. doi: 10.3390/biomedicines9121933
37. Barton, D. Improve Your Fertility With Vitamin C. 2021 Available from: https://natural-fertility-info.com/vitamin-c-to-improve-fertility.html
38. Choe J, Shanks AL, In Vitro Fertilization. [cited 2023 March 9] Available from: https://www.ncbi.nlm.nih.gov/books/NBK562266/
39. Crha I, Hrubá D, Ventruba P, Fiala J, Totusek J, Visnová H. Ascorbic acid and infertility treatment. Cent Eur J Public Health 2003;11(2):63-7.
40. Lunenfeld-Tanenbaum Research Institute: Researchers discover Vitamin C may impact fertility for generations. 2019. Available from: https://www.sinaihealth.ca/news/researchers-discover-vitamin-c-may-impact-fertility-for-generations/
41. Beyer RE. The role of ascorbate in antioxidant protection of biomembranes: interaction with vitamin E and coenzyme Q. J Bioenerg Biomembr 1994;26(4):349-58. doi: 10.1007/BF00762775
42. Conde-Agudelo A, Romero R, Kusanovic JP, Hassan S. Supplementation with vitamins C and E during pregnancy for the prevention preeclampsia and other adverse maternal and perinatal outcomes: a systematic review and metaanalysis. Am J Obstet Gynecol 2011;204(6):503.e1-503.12. doi: 10.1016/j.ajog.2011.02.020
43. West ChE, Dunstan J, McCarthy S, Metcalfe J, D'Vaz N, Meldrum S, Oddy WH, Tulic MK, Prescott SL. Associations between Maternal Antioxidant Intakes in Pregnancy and Infant Allergic Outcomes. Nutrients 2012;4(11):1747-58. doi: 10.3390/nu4111747
44. Ang A, Pullar JM, Currie MJ, Vissers MCM. Vitamin C and immune cell function in inflammation and cancer. Biochem Soc Trans 2018;46(5):1147-59. doi: 10.1042/BST20180169
45. Alesci A, Pergolizzi S, Fumia A, Miller A, Cernigliaro C, Zaccone M, Salamone V, Mastrantonio E, Gangemi S, Pioggia G, Cicero N. Immune System and Psychological State of Pregnant Women during COVID-19 Pandemic: Are Micronutrients Able to Support Pregnancy? Nutrients 2022;14(12): 2534. doi: 10.3390/nu14122534
46. Habibzadeh N, Schorah CJ, Smithells RW. The effects of maternal folic acid and vitamin C nutrition in early pregnancy on reproductive performance in the guinea-pig. Br J Nutr 1986;55(1):23-35. doi: 10.1079/BJN19860006