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# Vitamin C and its Role in Pregnant Ewes: Subject Review

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**Annotation:** It is an important antioxidant vitamin that helps protect cells from damage and water-soluble vitamins. It is important for the production of collagen, which is considered the main protein in connective tissues. Pregnancy in ewes represents a sensitive physiological period characterized by increased metabolic activity accompanied by an increased production of free radicals (Reactive Oxygen Species – ROS). This leads to oxidative stress, which can negatively impact the health of both the mother and fetus. Therefore, vitamin C (ascorbic acid) It is effective and important in neutralizing free radicals.

Although the liver of ruminants including sheep has the ability to synthesize vitamin C from glucose, scientific evidence suggests that this capacity may be insufficient during pregnancy, especially in the presence of external factors such as heat stress or malnutrition.

Studies indicate that adding vitamin C may improve biomarkers of oxidative stress, such as decreased malondialdehyde concentrations and increased activity of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, which contributes to protecting tissues from oxidative damage. While field research has shown that the

use of vitamin C supplements during pregnancy improves immune function in pregnant ewes by enhancing the response of lymphocytes and raising levels of IgG and IgM antibodies, which positively impacts the mother's resistance to disease and the transfer of passive immunity to the offspring.

From a reproductive perspective, supplementation reduced fetal absorption rates, improved lamb birth weight, and supported placental development, suggesting an indirect role of vitamin C in improving overall reproductive efficiency.

Results vary depending on the dose used and the period of administration. It has been shown that doses between 1-3 grams per day during the second half of pregnancy are the most effective without any apparent side effects. These data highlight the value of considering vitamin C but also as a supportive nutrient, but also as an important component of reproductive nutrition programs for pregnant ewes, especially in intensive production systems or harsh environmental conditions. When using of vitamin C can improve productivity in ruminants.

## Introduction

One of the antioxidant compounds in living organisms and a water-soluble vitamin, also called ascorbic acid.. Although ruminants, including ewes, have the ability to synthesize vitamin C endogenously in the liver via the glucose-to-ascorbic acid pathway,However, physiological conditions such as pregnancy, oxidative stress, and malnutrition may increase the demand for this vitamin to a degree that exceeds the endogenous capacity to synthesize it (Weiss, 2001; McDowell, 2000).

Pregnancy in ewes is accompanied by metabolic and physiological changes that lead to increased production of free radicals, increasing the oxidative burden on the organism. This oxidative stress can lead to cellular damage and disturbances in fetal development. As an antioxidant, vitamin C he has a role a pivotal role in protecting tissues from oxidative damage, enhancing maternal immunity, and improving placental function.

Pregnancy in ruminants, including ewes, is a critical physiological period characterized by significantly increased metabolic and nutritional requirements to support fetal growth, hormonal changes, and placental formation. During this phase, the body experiences elevated levels of oxidative stress.

It can be said that it is an imbalance between the production of free radicals and the body's ability to resist toxins. to neutralize them using the antioxidant defense system. This stress has been linked in numerous studies to pregnancy complications such as impaired fetal growth,

premature birth, increased miscarriage rates, and future fertility problems (Agarwal et al., 2005; Gupta et al., 2012). New studies point to the growing economic, environmental, and health challenges (particularly housing unavailability, productive sector efficiency, and heavy metal–induced environmental impacts) that plague Iraq and Kurdistan. Several studies have reported the advantages of supplemental minerals, such as selenium and zinc, on improving the productivity of animals and reducing the environmental pollution. In addition, there is a dimension of necessity for environmental aspects to complement the modern economic growth theories (Palani, 2025; Palani et al., 2025; Palani & Hussen, 2022; Palani et al., 2022a, 2022b, 2024a, 2024b). Accordingly, dietary antioxidants are receiving significant attention as supportive agents that promote metabolic balance and improve pregnancy outcomes. In this context, vitamin C stands out as one of the most important natural water-soluble antioxidants. Which plays a pivotal role in supporting the vital functions of the mother and fetus during pregnancy, through several mechanisms including reducing free radicals, enhancing immunity, stimulating collagen formation, and supporting the function of the placenta and blood vessels (Padayatty et al., 2003; Carr & Maggini, 2017).

**Chemical composition of vitamin C**

Albert Szen-Gyorgi was the first to discover vitamin C and won the Nobel Prize. In 1927, he isolated a sugar-like reducing agent from the adrenal gland, which he first called hexouronic acid. He also isolated this substance from plant sources, such as oranges, cabbage, and green peppers (Ayo et al., 2006).

It is a water-soluble organic compound belonging to the class of monocarboxylic acids containing a lactone group, and is structurally derived from glucose. Its molecular formula is $C_6H_8O_6$. It consists of a hexagonal carbon chain containing five hydroxyl groups, one of which is linked to a closed lactone ring. It is characterized by its chemical properties as a strong scavenger, as it readily donates electrons, giving it a high capacity to reduce free radicals.


**Figure (Vitamin C, chemical composition) Figure (Vitamin C, Nutrition with Formula)**

It exists in two forms: L-ascorbic acid, which is biologically active, and dehydroascorbic acid, an oxidized form that can be converted to the active form inside cells. This dynamic exchange between the reduced and oxidized form contributes to its support of antioxidant defense mechanisms in the body, It works by nteracting with free radicals such as superoxide radicals ($O_2^-$), hydroxyl radicals (OH), and peroxyl radicals, inhibiting the oxidative effects that lead to damage to cell membranes, DNA, and proteins (Ayo et al., 2006).

In addition, vitamin C enhances the re-repeat other antioxidants, such as vitamin E (alpha-tocopherol),by reactivating it to its reduced state after it has been oxidized, and it also plays a role in protecting vital components in the body from oxidation during periods of high oxidative stress such as pregnancy.

## Metabolism and production of vitamin C

Ruminants possess the enzyme L-gulonolactone oxidase (GULO), which is the key enzyme responsible for The last procedure in the conversion of glucose to ascorbic acid in the liver. This process begins with the conversion of glucose to D-glucuronic acid, which is then converted to L-gulonolactone and then to ascorbic acid by the enzyme GULO (Chatterjee, 1973).

Despite this internal construction, the rate of construction is not constant and is affected by numerous factors. Physiological stages, such as pregnancy or lactation, increase the need for vitamin C to support fetal growth and the formation of the placenta and tissues. Thermal and environmental stress, where the consumption of internal antioxidants increases due to Increased production of free radicals (Khan et al., 2016) Infection or inflammation, which requires an immune response that consumes ascorbic acid more (Carr & Maggini, 2017).

Since vitamin C is absorbed primarily in the ileum and jejunum by specialized sodium-dependent vitamin C transporters (SVCT1 and SVCT2), absorption is further complicated by microbial degradation in the rumen, which results in a significant portion of the vitamin C added to the diet being degraded before it is absorbed (Weiss, 2001).

Therefore, some studies prefer to administer vitamin C by non-oral means such as intramuscular or subcutaneous injection to ensure that it reaches the blood without microbial degradation, especially in the advanced stages of pregnancy (Hashem et al., 2018).

In a study, when added to the diet, it reduced the level of corticosterone in the blood, increased the secretion of thyroid hormone, and maintained metabolism and body temperature (Muhammed et al., 2023). As pregnancy progresses, the metabolic demand for vitamin C increases in ewes due to increased blood volume and increased circulation to nourish the fetus, the activity of reproductive and placental tissues, which rely on it for collagen formation and strengthening of blood vessels, and support of the immune defenses of the mother and fetus.

Studies have shown the positive effect of ascorbic acid in enhancing nutrients in digestion by activating digestive enzymes and thus improving the efficiency of food conversion (AL-Daloe et al., 2022).The liver stores a portion of vitamin C, but its storage capacity is limited, and excess is eliminated through urine. Therefore, the constant and increasing demand during pregnancy renders the liver permanently unable to meet its needs without external support (McDowell, 2000; Sies et al., 2017).

Ascorbic acid deficiency during pregnancy may lead to increased oxidative stress markers in the blood and placenta such as MDA malondialdehyde, decreased activity of antioxidant enzymes such as catalase and glutathione peroxidase, impaired fetal growth or intrauterine growth retardation (IUGR), and disturbances in placental formation or impaired nutrient transport (Abd El-Hamid et al., 2019; El-Shahat & Abdel Monem, 2011).

Multiple studies have shown that supplementation with vitamin C during pregnancy, particularly in the latter half, reduces oxidative stress, improves birth weight, reduces miscarriage, and improves immunity. However, the effectiveness of these supplements depends on several factors, such as dosage, chemical form, timing of administration, and delivery method (oral vs. injectable) (Yatoo et al., 2013; Khan et al., 2016).

## His tour of oxidation and other effects

Ascorbic acid works to reduce the oxidative effect due to its role in losing electrons to free radicals and it restores other antioxidants, Like glutathione and vitamin E, it enhances the immune system. Similar to oxidative stress in pregnant ewes, reactive oxygen species increase as a result of physiological changes after fertilization, leading to the destruction of lipids in plasma membranes, with increased damage to DNA and proteins (Castillo et al., 2005; Celi, 2011).

Some studies indicate that supplementing pregnant ewes with vitamin C resulted in a reduction in oxidative stress markers such as malondialdehyde concentrations and an increase in

antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase. (El-Deeb et al., 2020; Jafari et al., 2023).

Pregnant ewes are susceptible to diseases due to immune changes, while information indicates that vitamin C supports the function of white blood cells and stimulates the secretion of immune-stimulating cytokines (Weiss & Hogan, 2005). Experimental studies have shown that giving ascorbic acid to ewes during pregnancy improves macrophage responses and stimulates cellular immunity, reducing rates of inflammation and complications during pregnancy (Daramola & Adeloye, 2009).

While a study showed that ascorbic acid increased the bioavailability of iron from the digestive tract, which reduced oxidative damage that activates the hormone erythropoietin from the kidneys, which is responsible for the formation of red blood cells, which is important for preventing anemia during this stage (Omer and Alssadi, 2022).

Scientific evidence suggests that vitamin C supplements may reduce the risk of premature birth, low birth weight, and intrauterine growth retardation in ruminants (Duncan & Meyer, 2012). In a study, giving a daily dose of 1 gram of vitamin C to pregnant ewes during the last trimester of pregnancy resulted in reduced concentrations of oxidative stress markers, increased lamb birth weight, and decreased neonatal mortality during the first week (Abdelrahman et al. (2016).

The study showed that ascorbic acid also improves placental function and reduces the incidence of preeclampsia in ewes, a condition resulting from an imbalance between oxidants and antioxidants, Although vitamin C toxicity is rare in ruminants due to their ability to regulate its levels internally, excessive doses can lead to increased oxalate excretion in the urine. It helps prevent the buildup of salts in the urinary system, and is associated with the absorption of metals such as zinc and copper. It also speeds up oxidation rather than reduction when minerals are present in a state of continuous increase (Levine et al., 2001).

**Postpartum hormones and their effect on it**

The physiological process of lambing during labor is complex and is driven by a series of glandular signals, including prostaglandins, cortisol, and oxytocin. Changing the maternal feeding phase and the level of antioxidants directly influence the performance of this hormonal system during this condition, Antioxidants that influence hormonal balance during pregnancy through the action of vitamin C, either by reducing oxidative stress or through its indirect role on the endocrine system, are related to pregnancy.

Due to the increase in the amount of the hormone cortisol in the final stages of the fetus's position after the labor pain is activated, which leads to a follow-up of hormonal developments, despite the decrease in the hormone progesterone that protects the pregnancy, and the increase in the hormone estrogen that supports the rise in the clarification of oxytocin receptors in the uterus and the release of prostaglandin (F2α) that stimulates the muscle contractions of the uterus and increases the pain of labor directly, Kandiel et al (2015).

Studies have shown that a disturbance in the balance of the oxidative environment within the bodies of ewes may hinder or slow down birth, which gives antioxidants such as vitamin C a direct link and enhances its stages in reducing the levels of free radicals, which increase briefly and noticeably as the end of pregnancy approaches, and the tissues' response to the hormone oxytocin decreasesIt was shown in a study that providing vitamin C during the last two weeks of pregnancy to Awassi ewes resulted in a significant reduction in the concentration of the hormone oxytocin in the blood serum during the early stages of birth, a significant reduction in the concentration of the hormone cortisol related to stress, and an acceleration of the time of birth and a reduction in its duration compared to the control group, Kandiel et al. (2015).

It explains that ascorbic acid can support the uterus' response to oxytocin and accelerate labor. Prostaglandins are essential components in stimulating uterine contractions and rupturing the

corpus luteum to induce labor. A recent study by Mohamed et al. (2021) Experiments have confirmed that vitamin C's indirect mechanism of promoting prostaglandin production in the placenta depends on its localization in the lipid membranes of placental cells, which accelerates the enzymes responsible for prostaglandin synthesis and reductase.

While a study was conducted on twenty pregnant ewes when they were given one gram of vitamin C orally every day, an increase in prostaglandin and reductase levels in the plasma was shown one day before birth and a decrease in the rate of placental retention after birth.

Although the situation is a physiological process stimulated by inflammatory cytokines such as interleukin and tumor necrosis factor, it is likely that ascorbic acid regulates the interaction between these cytokines and reproductive hormones. I conducted an experiment by Al-Shanti et al. (2019) Pregnant ewes receiving vitamin C during the last 10 days of pregnancy experienced a reduction in interleukin and tumor necrosis factor levels, an increase in plasma estrogen and oxytocin levels, an improvement in delivery time, and an increase in the number of natural births without any other side effects. In context and support of this hypothesis, which states that vitamin C does not only work as an antioxidant, but its role as a coordinator of immunity and hormones is directly linked to the stability and safety of the labor process.

Most studies have shown that the optimal dosage of vitamin C for pregnant ewes ranges from 500 mg to 1 gram daily, starting from the last week or two of pregnancy until the day of delivery. It is preferable to administer it orally or intramuscularly to ensure rapid absorption. Although considered safe, very high doses should be avoided, as they inhibit copper absorption or cause electrolyte imbalance.

When added to pregnant ewes' feed, it has been shown to positively impact birth weight, vital organ development, and postpartum survival. This indicates its ability to enhance collagen formation, improve iron absorption, and develop blood vessels in the placenta, thereby increasing the efficiency of nutrient exchange between mother and fetus.

While administering 200 mg/kg of vitamin C to ewes in the second week of the fourth month of pregnancy resulted in a 12% increase in birth weight and an increase in the vital activity of newborns within the first 24 hours after birth. It also demonstrated its role in reducing fetal mortality rates resulting from preeclampsia or placental insufficiency Salem et al (2020).

However, its prominent role in stimulating intrauterine growth retardation (IUGR) by reducing inflammation and inhibiting harmful cytokines.

**Optimal dosage of vitamin C in pregnant ewes**

The appropriate dose of vitamin C for pregnant ewes ranges from 100 to 500 mg/kg live weight per day, depending on the animal's environmental and physiological conditions. An experiment was conducted by Khan et al, (2017) on pregnant ewes where they were dosed with ascorbic acid orally at doses up to 250 mg/kg/day, which resulted in a clear improvement in reproductive performance measures such as increased pregnancy change and enhanced birth weight. An experiment conducted by researchers Al-Khalifa et al. (2020) demonstrated the role of three different amounts of vitamin C (0, 150, and 300 mg/kg of body weight) during the last three months of pregnancy. The average amount (150 mg/kg) helped reduce oxidative stress and enhance blood immune indicators, but the highest amount (300 mg/kg) did not show any noticeable effects, which is evidence that a higher amount may remain effective without the benefit of other supplements.

While its physiological effects help reduce free radicals resulting from increased metabolic processes during pregnancy, it also has a role in protecting proteins and cell membranes from oxidative damage, Badiati et al. (2003) It also activates collagen, which is necessary for building the fetal membranes and placenta, and supports the digestive system in absorbing iron, thus helping to prevent anemia during pregnancy, It also has an effect on regulating the immune

system, while avoiding miscarriages resulting from infection or excessive oxidative stress (Ali et al., 2019).

The studied dose also contributed to improved fetal survival rates and reduced miscarriage rates (Nwobodo et al., 2021), increased birth weight and improved fetal vitality, and reduced stress markers within the amniotic fluid, indicating a protective and protective role for the fetus (Wang et al., 2020). Since interactions with other antioxidants indicate that administering vitamin C with other antioxidants, such as vitamin E or selenium, may have a synergistic effect in reducing oxidative damage during pregnancy. In a study by Abdelrahman & Kamel (2022), it was found that combining vitamins C and E reduced blood levels of malondialdehyde (MDA), an indicator of oxidative stress, more effectively than giving either of them alone.

While the risks of overdosing are relatively safe due to its water solubility and the ability to eliminate excess nutrients through urination, some studies have warned of overdosing (hypervitaminosis C), which may negatively affect mineral balance, especially copper and zinc, or cause diarrhea and increased urinary calcium excretion (Carr & Frei, 1999). Therefore, the dosage should be confirmed and the animal's health status assessed before initiating supplementation.

**Its role in fetal life and newborn growth**

Ascorbic acid is a vital nutrient important for pregnancy physiology, fetal development, and immune system function. Although ruminants, such as ewes, can synthesize vitamin C endogenously in the liver, harsh physiological conditions, such as pregnancy, may require additional amounts to compensate for increased consumption, especially during rapid fetal growth.

It participates in many vital processes essential for fetal development, including the formation of collagen, a key component of connective tissues, including blood vessels, cartilage, and skin. It has another effect, such as enhancing many enzymatic reactions that help build hormones and neurotransmitters, which are very important for the development of the fetus's nervous system.

An experiment indicated that adding 30 mg/kg of vitamin C to the animal's body weight during the last third of pregnancy in sheep resulted in supporting the quality of the placenta and contributed to an increase in the weight of lambs at birth compared to the control group (El-Ashry et al., 2003).

Increased oxidative stress resulting from the physiology of pregnancy in multiparous ewes, resulting from increased metabolic parameters and tissue oxygen demand, where ascorbic acid plays a strong and powerful role as an antioxidant to reduce free radicals, which reduces oxidative damage to placental and fetal cells, Researchers confirmed in their study, Abdul Rahman et al., (2020). that in the case of providing vitamin C with vitamin E, it significantly reduced the parameters of oxidative stress in pregnant ewes and preserved the life of the fetus in the womb until the end.

An experiment demonstrated the role of vitamin C in stimulating growth while supporting placental function, expanding placental blood flow and thus developing and providing nutrients to the fetus. It also had an effect on lambs born to ewes that received vitamin C, with high weights. The development of growth markers in the first month of life (Khalifa et al., 2013) may help in the formation of collagen in the blood vessels of the fetus and the placenta.

Vitamin C deficiency in ewes during pregnancy is linked to a high rate of premature birth, especially in an environment exposed to high temperatures with poor nutrition, according to veterinary studies (Hernandez et al., 2011), which helps preserve the placenta and avoid premature rupture of the membranes.

Consuming large amounts of copper may lead to negative effects such as impaired copper absorption or increased urination. However, most studies confirm that the optimal intake for

pregnant women is between 20 and 40 mg/kg of body weight per day, particularly during the last three months (Sahin et al., 2009). This dose varies depending on the animal's condition.

## Conclusions

Vitamin C is an important nutrient that helps enhance the physiological reproductive performance of pregnant ewes, usually during the last three months of pregnancy, because this is a critical period for the completion of vital processes connected to the completion of the construction of the fetus's body, The placenta doubles in size and stimulates the endocrine glands in preparation for delivery. New scientific studies demonstrate that vitamin C goes beyond its antioxidant role to include more complex biological pathways, such as regulating hormone secretion, protecting the placental membranes, and supporting the immune system of the fetus and mother, It also contributes to the health of pregnant ewes, both in terms of internal physiology and birth outcome.

This vitamin is considered an important element in protecting pregnancy stability, hormonal balance, fetal development, and reproductive activity, making it a valuable nutritional factor in the diet of pregnant ruminants. Evidence suggests that vitamin C enhances the development of the internal environment of pregnant ewes through a variety of integrated pathways and also helps maintain a balance between antioxidants and their cofactors. This oxidative stress increases during pregnancy due to increased metabolic activity and growth of the placenta and fetus, and enhances the metabolic suitability of active elements such as iron, phosphorus and calcium. It directly affects the mother's health and the growth of the fetus. These actions also complement its role in protecting the placenta from dispersion by contributing to the production of collagen and supporting tissue elasticity while maintaining the health of blood vessels.

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