Study of thymus development in sheep during the postnatal period of ontogenesis in EL-Oued province, Algeria.

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Received: 29 September 2024 /Accepted: 15 November 2024 /Published online: 17 December 2024.

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Abstract

The study of the immune system remains a critical issue in veterinary science, with the thymus being a central organ in immunogenesis. It plays a key role in both cellular and humoral immunity and produces various biologically active substances. This article examines the structural changes in the thymus of sheep across different age stages, from birth to nine months, with a focus on the effects of the biologically active. The study observes the dynamics of changes in the parenchyma and stroma components of the thymus. Findings indicate that the relative area of the thymus parenchyma increases with age, particularly due to the growth of the cortical zone. Furthermore, sheep treated exhibited an enhanced lymphoid tissue presence in the thymus, suggesting that the positively influences the development of lymphoid organs.

Keywords: age, development, structural, thymus, sheep.

Citation: Rahmoun D.E., Zeghdani M.A., Laadjailia Y. Study of Thymus Development in sheep during the postnatal period of ontogenesis in El-Oued province, Algeria. Algerian International Veterinary journal 2024, 0, 15-21. https://www.univ-soukahras.dz/en/revue/aivj

Introduction

The thymus is a central organ in the immune system, primarily responsible for the maturation of T-lymphocytes (T-cells), which are essential for cellular immunity. As a primary lymphoid organ, the thymus plays a critical role in immune defense, particularly in the development of the T-cell repertoire that allows for immune tolerance and pathogen recognition. The thymus has a conserved basic structure across species, but there are notable variations depending on factors such as species, age, and physiological condition. The thymus is enclosed by a connective tissue capsule, and its internal structure is divided into lobules by septa that extend inward from the capsule. Each lobule is composed of two distinct regions: the cortex and the medulla. The cortex is densely populated with immature thymocytes (precursor T-cells), which undergo differentiation and positive selection. These thymocytes are supported by epithelial reticular cells, which play a critical role in T-cell maturation by providing structural support and secreting factors like cytokines and growth factors essential for thymocyte differentiation (Liu et al., 2019).The medulla contains mature thymocytes that have successfully passed through the selection process in the cortex. The medullary region is further characterized by Hassall's corpuscles, which are spherical or ovoid structures composed of keratinized epithelial cells. While the exact function of these structures is still debated, they are believed to be involved in the induction of central tolerance by eliminating self-reactive T-cells (Liu et al., 2019). A distinctive feature of the thymus is the blood-thymus barrier, which consists of specialized endothelial cells, a thick basal lamina, and epithelial reticular cells. This barrier protects the developing thymocytes from being exposed to circulating antigens and ensures that thymocytes undergo strict selection within the thymus itself. This is critical for the development of T-cells that can distinguish between self and non-self antigens, thereby preventing autoimmune reactions (Janeway et al., 2001).

The thymus is most active during the neonatal and juvenile stages, when it is responsible for producing a high number of T-cells. This stage is essential for establishing the immune system and ensuring that a diverse population of T-cells is available to recognize a wide range of pathogens. However, after this peak activity period, the thymus begins to undergo involution, a process in which the size of the organ decreases and its functional tissue is replaced by adipose (fat) tissue. Thymic involution is a natural part of aging and occurs at different rates depending on the species. In humans and many mammals, thymic involution begins after puberty, but some animals, such as camels and certain primates, experience slower involution (Gordon et al., 2000).

Despite thymic involution, the organ continues to play a vital role in the production of T-cells throughout life, albeit at a diminished rate. The decline in thymic function with age contributes to a reduced diversity of the T-cell repertoire and may explain the increased vulnerability to infections and certain diseases in older animals (Berg et al., 2007). The thymus plays a central role in both cellular immunity (through T-cells) and humoral immunity (indirectly by interacting with other immune cells like B-cells). T-cells that mature in the thymus perform a variety of immune functions: Helper T-cells (CD4+): These cells coordinate the immune response by activating other immune cells, such as macrophages and B-cells, to respond to infections (Abbas et al., 2017). Cytotoxic T-cells (CD8+): These cells directly kill infected or cancerous cells by recognizing specific antigens presented on the surface of infected cells (Waldman et al., 2020). The thymus ensures that only T-cells with functional receptors for self-major histo compatibility complex (MHC) molecules survive, while those that react too strongly to self-antigens undergo apoptosis. This process is known as negative selection and is crucial for maintaining immune tolerance and preventing autoimmune diseases (Zhu et al., 2015). Interestingly, more than 90% of thymocytes undergo apoptosis during development due to failure in passing the selection processes (Berg et al., 2007). While the general structure and function of the thymus are conserved across species, there are notable differences in its location, shape, and size in different animals. In birds, the thymus is typically located along the neck, often in the form of an elongated structure (Shakhov et al., 2018). In ruminants such as sheep, goats, and cattle, the thymus is often larger, and the medullary region contains well-developed Hassall’s corpuscles (Kharitonov et al., 2012). In contrast, rodents and lagomorphs (like rabbits) exhibit a thymus structure with clear delineation between the cortex and medulla but a less pronounced presence of Hassall’s corpuscles. For example, the thymus in rodents is more compact, and although it undergoes involution, the process is slower than in some larger mammals (Kawamoto et al., 2011). For camels, thymic structure also shows species-specific variations, including a well-developed medullary region and a prominent presence of Hassall's corpuscles. This may reflect adaptations to their environment, where immunity is highly specialized for resistance to pathogens common in arid regions (Mora et al., 2014). Thymic health and development are critical for the proper functioning of the immune system. Any disruptions to thymic function, whether due to age, disease, or environmental factors, can result in immunodeficiency or autoimmunity. Research has shown that interventions such as nutritional supplementation or hormonal treatment can affect thymic size and function, potentially enhancing the immune response in certain species (Ostuni et al., 2018). In veterinary medicine, understanding the dynamics of thymic development and involution is crucial for addressing immune disorders in animals. For instance, immune-mediated diseases in animals often involve abnormal thymic function or T-cell dysregulation, and interventions that modulate thymic activity can have therapeutic potential (Mackey et al., 2015). The thymus is an essential organ for T-cell maturation and immune system function. Its structure is conserved across species, although there are species-specific adaptations that reflect the unique immunological needs of different animals. The thymus remains critical for immune surveillance throughout life, even as it undergoes involution with age. The study of thymic function, especially in relation to thymic involution and age-related immune decline, provides valuable insights into the aging immune system and may offer therapeutic avenues for enhancing immune responses in both animals and humans.

Materials and methods

The study used newborn, two-month-old, five-month-old, and nine-month-old sheep from private farms in the El Oued region Algeria. The experiment involved the use of the development which development effects. to the sheep observed and examination by histological slide at different age 1, 2, 4, and 5 months.

The relative area of the thymus components (parenchyma and stroma) was measured using micro morphometric techniques. For histological analysis, tissue samples were fixed in neutral formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Statistical data analysis was performed.

The relative area of parenchyma in experimental sheep showed an increase with age, especially in comparison to the control group, with the experimental group showing more pronounced development in the thymus. The cortical zone (outer layer) showed a similar trend, with significant increases in the experimental group at various age stages, especially in the 9-month-old sheep. In the medulla, both control and experimental groups exhibited increases, but the experimental group demonstrated a more substantial rise in lymphoid tissue compared to the control group. The stroma (supporting tissue) decreased over time, particularly in the experimental group, indicating changes in the thymus structure in response to the "Gamavit" treatment. The capsule and trabeculae (connective tissue structures) also showed slight variations in their relative area, with some differences between the control and experimental groups, though the changes were less pronounced compared to other thymus elements. The development of the thymus, particularly by increasing the lymphoid tissue area and improving the structural integrity of the thymus in sheep across different age stages.

Results

These results highlight the differences between the two groups, with the experimental group generally showing enhanced growth and slower involution in key thymic structures compared to the control. The specific experimental conditions leading to these results would provide further insight into how thymic development and immune function can be influenced by external factors.

The study on thymic development in lambs over a period from birth to 9 months compared two groups: a control group and an experimental group. Both groups showed an overall increase in the relative area of the thymus, with the experimental group demonstrating slightly more growth. By 2 months, the experimental group showed a 9.7% increase in relative thymic area, compared to 9.0% in the control group. From 5 to 9 months, the experimental group continued to show more growth (2.2% vs. 0.6%) and, by 9 months, had a 16.9% increase in thymic area compared to 11.4% in the control group.

Despite this initial growth, both groups experienced a decrease in thymic area over time. The experimental group showed a more significant overall decrease (4.5% vs. 1.3%), suggesting a greater rate of involution. Specifically, the stroma (the supporting tissue of the thymus) showed a decrease over time, with the experimental group exhibiting a more pronounced reduction. The capsule area decreased by 5.4% in the experimental group versus 3.3% in the control group by 9 months, while the trabeculae area decreased in both groups, with a slightly larger reduction in the experimental group (7.0% vs. 6.8%).

Notably, the experimental group exhibited greater overall thymus growth or slower reductions in certain structures, particularly in the thymic parenchyma and cortex, suggesting that whatever intervention was applied to the experimental group had a positive effect on thymus development and function. The findings of this study suggest that the experimental conditions may influence thymic morphology in a way that supports continued lymphoid tissue development and function, even as the thymus begins its natural involution process. The results are presented in table 01.

Table 01: the structural components of the Thymus in Sheep (x±m), n=5

Time Period	Control Group Increase in Thymic Area	Experimental Group Increase in Thymic Area	Control Group Decrease in Area	Experimental Group Decrease in Area
Birth to 2 months	10.1%	10.7%	N/A	N/A
2 to 5 months	N/A	N/A	N/A	N/A
5 to 9 months	0.6%	2.2%	N/A	N/A
9 months	11.4%	16.9%	1.3%	4.5%
Capsule Reduction	3.3%	5.4%	N/A	N/A
Trabeculae Reduction	6.8%	7.0%	N/A	N/A

The study examines the development of the thymus in lambs over a period from birth to 9 months, comparing the control. The relative area increased in both groups, with the experimental group showing slightly more growth (9.7% vs. 9.0% by 2 months and 2.2% vs. 0.6% from 5 to 9 months). Both groups showed significant initial growth (10.1% in controls, 10.7% in the experimental group by 2 months). The experimental group continued to show more growth overall (16.9% vs. 11.4%

by 9 months). The area decreased in both groups, but the experimental group showed a more significant overall decrease (4.5% vs. 1.3%). The stroma decreased over time, with the experimental group showing a slightly more pronounced decrease in both the capsule and trabeculae.The capsule area decreased, with a 5.4% reduction in the experimental group versus 3.3% in the control group by 9 months.The trabeculae area decreased in both groups, with the experimental group showing a slightly more substantial reduction (7.0% vs. 6.8%).The experimental group generally exhibited greater thymus growth or slower reductions in some structures compared to the control group, particularly in the thymus parenchyma and cortex. The results of the study are presented in the Graph below.

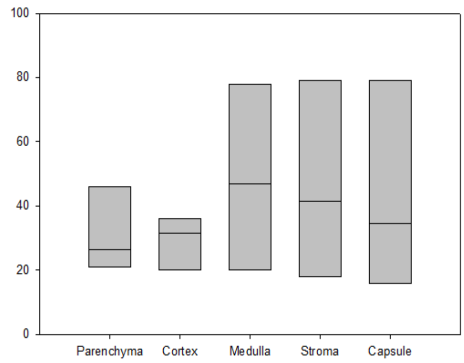

Figure 1: Graph represents the structural components of the Thymus in Sheep (x±m), n=5.

Discussion

In lambs, the thymus undergoes significant morphological changes during postnatal development. The relative area of the thymic parenchyma (the functional tissue of the organ) increases from birth to nine months, with a more pronounced increase in the experimental group compared to the control group. This developmental trend highlights the dynamic nature of thymic growth and its association with immune system maturation.

The increase in the thymic parenchyma is primarily attributed to the cortex, where immature T-lymphocytes (thymocytes) undergo differentiation and selection. The relative growth rate of the cortex was consistently higher in the experimental group, particularly between birth to two months and again from five to nine months. The early phase of growth (birth to two months) coincides with the critical period of thymic function in neonatal lambs, as it is during this time that a large influx of thymocytes is recruited. A similar pattern of thymic growth is observed in other species such as goats and cattle during early life (Smith et al., 2014).

The medulla, on the other hand, showed a decrease in relative area until the lambs reached five months of age, reflecting the maturation of thymocytes into functionally competent T-cells. The reduction in medullary area was more prominent in the experimental group, particularly between birth and two months, and again from five to nine months. This decline in the medulla may be related to the maturation of T-cells that exit the thymus and migrate to peripheral lymphoid tissues (Shah et al., 2020).

The thymic stroma, which includes the capsule and trabeculae (trabecular connective tissue), also experienced a decrease in relative area as lambs aged. The reduction in stroma was more pronounced in the experimental group, indicating that the structural framework of the thymus may undergo remodeling as the organ matures and its functional activity evolves. In ruminants like cattle and goats, similar changes in the stroma are observed, with a decline in the relative area of thymic stroma as the lymphoid tissue becomes more specialized in T-cell production (EL HAFEZ et al., 2023).

This increase in thymic parenchyma during early development is followed by a phase of thymic involution after around five months, which is consistent with patterns observed in other mammalian species. Thymic involution is characterized by a reduction in the production of new thymocytes and an increase in thymic adiposity (Andreotti et al., 2010). In lambs, this process accelerates after nine months, with a significant decline in the thymic cortex, especially in the control group, and a higher percentage of fatty tissue replacing functional thymic tissue.

The experimental group showed a more significant increase in the thymic cortex and a greater decrease in the medulla and stroma compared to the control group. These changes might be due to experimental interventions, such as nutritional factors, hormonal treatments, or environmental stressors, which can influence thymic development and immune function. Studies have shown that factors such as diet, disease exposure, and stress can affect thymic structure and function (Bahlol et al., 2018). For example, experimental malnutrition or exposure to certain growth factors may stimulate thymic hyperplasia or, conversely, cause premature involution (Egawa et al., 2005).

Conclusion

The study concluded that the relative area of the thymic parenchyma in lambs increased more significantly due to the cortex in the experimental group, which received "Gamavit." The absolute measurements of the thymic lymphoid tissue in the experimental group were higher at all age points compared to the control group, indicating more significant thymus development in the experimental animals.

Acknowledgements

We would like to express our sincere gratitude to the Institute of Veterinary Sciences of Taoura and the Histology Laboratory for their invaluable assistance and support throughout the course of this study.

Conflict of interest: The authors declare that they have no conflicts.

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