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ORIGINAL ARTICLE

Age-Related Changes in the Human Thymus Gland: A Comparative Study of 70 Specimens

SHAHID KAMRAN[1], MUHAMMAD YOUSUF KHOSO[2], SALEEM AHMED BHUTTO[3], IRFAN UL AKBAR[4], IMRAN MEHBOOB BAIG[5], SYED IRFAN RAZA ARIF[6]

[1]*Associate Professor, Forensic Medicine, Al-Tibri Medical College Karachi*
[2]*Assistant Professor Pathology, Al-Tibri Medical College Karachi*
[3]*Assistant Professor, Anatomy, Frontier Medical and Dental College Abbottabad*
[4]*Assistant Professor, Physiology, Sahara Medical College, Narowal*
[5]*Assistant Professor, Physiology, Shahida Islam Medical College, Lodhran*
[6]*Associate Professor Anatomy, Bashir College of Dentistry, Islamabad*
Correspondence to: Muhammad Yousuf Khoso, Email: alatifj55@hotmail.com

ABSTRACT

Background: The thymus gland is a central organ for the development of T-cells, integral to the immune system. Its function significantly changes with age, leading to alterations in immune response, a phenomenon referred to as thymic involution.

Objective: This study investigates the structural and functional alterations in the thymus gland of 70 specimens from individuals across various age groups to identify the effects of aging on thymic morphology and function.

Methods: A total of 70 human thymus specimens were collected from individuals ranging from newborns to individuals over 70 years of age. Tissue samples were analyzed for size, weight, histology, and immune function. Immunohistochemistry and T-cell quantification were used to assess the presence of thymocytes and thymic epithelial cells.

Results: The study found a significant decline in thymic size, cellular composition, and thymocyte production with age. In older individuals, thymic tissue was largely replaced by adipose tissue, and the medullary region exhibited reduced cellular organization. T-cell output was found to be drastically reduced in individuals over 60.

Conclusion: The thymus undergoes substantial morphological and functional decline with aging, contributing to immunosenescence. These findings underline the importance of maintaining thymic function and suggest potential therapeutic strategies for thymic rejuvenation in elderly populations.

Keywords: Thymus gland, age groups, T-Cell Quantification

INTRODUCTION

The thymus gland is a primary lymphoid organ essential for the maturation and differentiation of T-cells, which are crucial for the adaptive immune response. Throughout early life and adolescence, the thymus is highly active, producing a diverse pool of naïve T-cells that protect against infections and maintain immune homeostasis. However, with aging, the thymus undergoes progressive involution, a process in which functional thymic tissue is replaced by adipose tissue, leading to a reduction in thymic output[1].

Thymic involution is characterized by several age-related changes, including decreased thymic size, a reduction in thymocyte populations, and a decline in the organ's ability to generate new T-cells[2]. This decline is thought to contribute to immunosenescence, the age-related decline in immune function, which increases susceptibility to infections, cancer, and autoimmune diseases[3].

Despite the critical role of the thymus in aging immunity, the exact mechanisms underlying thymic involution and the specific changes that occur at the cellular and molecular levels remain poorly understood. Recent studies have highlighted that the involution process may vary between individuals, with some showing more pronounced reductions in thymic function than others[4,5]. This variation could be linked to genetic factors, hormonal influences, and lifestyle factors such as nutrition and physical activity[6].

The present study aims to systematically investigate the histological and functional changes that occur in the thymus gland with age, analyzing 70 specimens from individuals ranging from infancy to old age. By examining the relationship between thymic size, cellular composition, and immune function, this study seeks to provide a comprehensive overview of age-related changes in the thymus and their implications for immune health in older adults.

METHODOLOGY

This cross-sectional study was designed to analyze the morphological, histological, and functional changes in the thymus gland across 70 human specimens collected from individuals in five distinct age groups: infants (0-2 years), children (3-12 years), young adults (18-30 years), middle-aged adults (40-60 years), and elderly adults (60+ years). The study was conducted at Frontier Medical and Dental College Abbottabad/ Al-Tibri Medical College Karachi during from the period October 2022 to September 2023.

Inclusion and Exclusion Criteria:

. Inclusion Criteria:
. Human thymus specimens from individuals of various age groups, ranging from 0 to 80 years.
. Individuals with no known autoimmune diseases or history of cancer.
. Specimens collected post-mortem under ethical guidelines, with appropriate consent from relatives.
. Exclusion Criteria:
. Specimens from individuals with chronic inflammatory diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus).
. Individuals with history of chemotherapy or other immunosuppressive treatments.
. Individuals with documented thymic disorders or congenital abnormalities.

Data Collection:

. Thymus Size and Weight: Each specimen was carefully measured for its length, width, height, and weight. The volume was calculated using the formula for a rectangular prism, while the weight was recorded with a precision scale.
. Histology: Tissue samples were processed and embedded in paraffin blocks. Sections of 5 µm thickness were stained with H&E (hematoxylin and eosin) and immunohistochemistry (IHC) for specific markers such as CD3 for thymocytes and cytokeratin for thymic epithelial cells.
. T-cell Quantification: Immunohistochemical staining for CD3 (marker for T-cells) and cytokeratin (for epithelial cells) was used to assess the density and distribution of thymocytes and epithelial cells across the thymus. The number of T-cells in the cortex was quantified by counting the number of positive cells in five random fields per slide.

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Data Analysis: Statistical analysis was performed using SPSS software (Version 27). The following analyses were conducted:

. Descriptive Statistics: To summarize the demographic data, thymus size, weight, and cellular composition across age groups.
. Logistic Regression: Used to determine the association between age and thymic involution. The logistic regression model included age as the independent variable and thymocyte density as the dependent variable.
. Chi-square Tests: To assess the association between age and the presence of adipose tissue in thymus specimens.

RESULTS

A total of 70 human thymus specimens were analyzed in this study. The specimens were obtained from individuals in five distinct age groups: infants (0-2 years), children (3-12 years), young adults (18-30 years), middle-aged adults (40-60 years), and elderly individuals (60+ years). The study included 30 male specimens (42.9%) and 40 female specimens (57.1%).

The distribution of specimens across the age groups was as follows: 10 specimens from infants (5 males, 5 females), 15 specimens from children (8 males, 7 females), 20 specimens from young adults (10 males, 10 females), 15 specimens from middle-aged adults (7 males, 8 females), and 10 specimens from elderly individuals (4 males, 6 females).

Thymus size and weight decreased significantly with age. In infants, the thymus was large, with an average size of 16.2 cm³ and a weight of 22.3 g. By the time individuals reached their elderly years, the thymus had significantly shrunk, with an average size of 4.3 cm³ and a weight of only 5.7 g.

Table 1: Demographical Details

Age Group	Number of Specimens	Males	Females
Infants (0-2 years)	10	5	5
Children (3-12 years)	15	8	7
Young Adults (18-30 years)	20	10	10
Middle-aged Adults (40-60 years)	15	7	8
Elderly (60+ years)	10	4	6
Total	70	30	40

Table 2: Thymus Size and Weight Across Age Groups

Age Group	Mean Thymus Size (cm³)	Mean Thymus Weight (g)
Infants (0-2 years)	16.2	22.3
Children (3-12 years)	14.5	18.5
Young Adults (18-30 years)	10.4	12.1
Middle-aged Adults (40-60 years)	7.6	8.3
Elderly (60+ years)	4.3	5.7

As shown in the table, thymus size and weight progressively decrease with age, with the most notable reduction observed in the elderly group ($p < 0.05$).

Histological analysis revealed a progressive shift in thymic structure with age. In infants and children, thymic tissue was densely populated with thymocytes. The cortex was thick, and the medulla was well-organized with minimal fat infiltration. As individuals aged, there was an increase in adipose tissue, and the thymus exhibited thinning of the cortex and more disorganized medullary regions. In the elderly, the thymus was predominantly adipose tissue with few thymocytes present.

Table 3: Histological Findings and Thymocyte Density Across Age Groups

Age Group	Thymus Architecture	Adipose Tissue Infiltration	Thymocyte Density (%)
Infants (0-2 years)	Dense thymocytes, well-organized	Minimal	80%
Children (3-12 years)	Densely packed, minor changes	Minimal	75%
Young Adults (18-30 years)	Thymocyte density decreases	Mild adipose infiltration	60%
Middle-aged Adults (40-60 years)	Thymocyte density low	Moderate adipose infiltration	40%
Elderly (60+ years)	Few thymocytes, disorganized	High adipose infiltration	20%

Thymocytes were abundant in infants and children but significantly reduced in elderly individuals. The cortex of the thymus became thinner and less organized as individuals aged, especially in those over 60.

Immunohistochemical analysis of T-cells (CD3) showed a marked reduction in thymocyte density with age. Infants had the highest density of CD3-positive cells, with nearly 80% of the thymus cortex populated by thymocytes. In elderly individuals, this number dropped to less than 20%.

Table 4: T-cell Quantification Across Age Groups

Age Group	CD3-positive Thymocyte Density (%)
Infants (0-2 years)	80%
Children (3-12 years)	75%
Young Adults (18-30 years)	60%
Middle-aged Adults (40-60 years)	40%
Elderly (60+ years)	20%

This significant decrease in thymocyte density correlates with the decline in thymus function as individuals age, resulting in reduced T-cell production and a diminished immune response.

Logistic Regression Analysis: Logistic regression analysis was performed to assess the relationship between age and thymus parameters, particularly thymocyte density. The model considered age as the independent variable and thymocyte density as the dependent variable. The results showed that age was a significant predictor of thymocyte density, with each decade of life reducing the likelihood of high thymocyte density by approximately 13%.

The negative coefficient for age indicates that with each year of age, the odds of having higher thymocyte density decrease. The odds ratio of 0.87 suggests that for every additional decade, the probability of having a high density of thymocytes decreases by 13%. Thymus size and thymocyte density both significantly influenced immune function in aging individuals.

Table 5: Logistic Regression Analysis for Thymus Parameters

Variable	Coefficient	Standard Error	p-value	Odds Ratio
Age	-0.13	0.04	0.002	0.87
Thymus Size	0.15	0.05	0.009	1.16
Thymocyte Density	-0.22	0.07	0.004	0.8

DISCUSSION

The results of this study underscore the progressive decline in thymic size, thymocyte density, and T-cell production with age. Thymic involution, beginning in early adulthood, accelerates with advancing age, leading to significant functional impairment in the thymus. This decline correlates with immunosenescence, as reduced thymic output compromises the immune system's ability to respond to novel pathogens and maintain immune tolerance[7].

The findings are consistent with previous research on thymic aging, which shows that the involution process is driven by both intrinsic factors such as hormonal changes and extrinsic factors such as chronic inflammation[8,9]. Studies have also highlighted the role of thymic epithelial cells in thymic function, with aging contributing to their decreased ability to support T-cell differentiation[10]. The reduction in naive T-cell production in older adults has important clinical implications, as it affects the body's response to vaccines and increases susceptibility to infections and autoimmune diseases[11,12].

Recent studies have proposed various strategies for counteracting thymic involution, including thymic regeneration

therapies and stem cell-based interventions[13,14]. However, the challenge remains in developing therapies that can effectively restore thymic function without compromising the immune system's balance.

Additionally, while this study provides robust evidence of the age-related changes in the thymus, it is important to note some limitations. First, the study is cross-sectional in nature, which limits the ability to draw conclusions about causality. Longitudinal studies tracking thymus changes over time would be beneficial to further understand the dynamics of thymic involution. Moreover, the sample size, while appropriate for an exploratory study, could be expanded to include more specific subgroups (e.g., individuals with specific chronic diseases or those with different lifestyles) to assess the impact of these factors on thymic involution.

In summary, our findings contribute to the growing body of evidence on thymic involution and immunosenescence. The progressive decline in thymic size and function with age underscores the importance of the thymus in maintaining immune health throughout life. The reduction in thymocyte density and the increasing presence of adipose tissue are clear markers of this involution, and the logistic regression analysis confirms that age is a key predictor of these changes. Understanding the mechanisms of thymic aging and the potential for therapeutic interventions remains a crucial area for future research.

CONCLUSION

In conclusion, the thymus undergoes significant involution as individuals age, characterized by a reduction in size, weight, thymocyte density, and an increase in adipose tissue. These changes contribute to the decline in immune function and are strongly associated with age, as shown by the logistic regression analysis. Thymic involution leads to reduced T-cell production, which in turn contributes to immunosenescence, leaving elderly individuals more susceptible to infections and less responsive to vaccinations.

Our study supports the hypothesis that thymic aging plays a critical role in the decline of immune function with age. The association between thymic size, thymocyte density, and age highlights the importance of thymic function in maintaining adaptive immunity throughout life. Future research focused on developing therapeutic strategies to slow or reverse thymic involution, such as stem cell-based therapies or thymic hormone treatments, could provide promising avenues for enhancing immune function in older populations. Understanding the precise mechanisms behind thymic involution and identifying potential interventions to restore thymic function will be essential for improving the health and quality of life of aging individuals.

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