

Human Thymus Gland in Young and Old Age; A Comparative Study

SYEDA RIZWANA JAFRI¹, UZMA WASEEM², SAMIA SHAHBAZ³, SADIA WAZIR KHAN⁴, AMNA MUNEEB⁵, AMNA REHMAN⁶

¹Assistant Professor, Anatomy Dept, Azra Naheed Medical College, Lahore

²Assistant Professor Anatomy, Shalamar Medical and Dental College, Lahore

³Senior Demonstrator, Anatomy, Shalamar Medical and Dental College, Lahore

⁴Lecturer of Anatomy Basic Medical Sciences Department, College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia.

⁵Senior Demonstrator Anatomy, Azra Naheed Medical College, Lahore

⁶Senior Demonstrator Anatomy, Central Park Medical College, Lahore

Corresponding author: Syeda Rizwana Jafri, Cell No: 03336893848

ABSTRACT

Aim: Research was undertaken to compare the findings between patients of different ages in terms of human thymus gland parameters.

Study Design: Comparative/observational study

Place and study: This study was conducted at anatomy department of Jinnah Hospital, Services Hospital and General Hospital Lahore during the period from November 2013 to October 2014.

Methods: Total 70 specimens of human thymus of 54 patients were enrolled in this study. All specimens were divided in to two groups I and II, Group I contains 35 patients with ages < 30 years and group II with 35 patients having ages 45 to 60 years. All specimens were fixed in 10% formalin solution and then processed for paraffin embedding. Compare the different parameters such as thickness of interlobular connective tissue and thymic capsule, length and number of Hassal's corpuscles between both groups. Data was analyzed by SPSS 23.0.

Results: In group I mean age of the patient was 24.16±3.43 years with mean BMI 21.55±6.37 kg/m² and in group II mean age was 52.11±2.87 years with mean BMI 25.07±4.39 kg/m². There was a significant difference observed between both groups regarding thickness of interlobular connective tissue and thymic capsule, quantity and length of Hassal's corpuscles with p-value <0.05.

Conclusion: As a result of this study, it can be inferred that younger patients had a substantially thinner thymic capsule and interlobular connective tissue, as well as more and smaller Hassal's corpuscles, than older patients.

Keywords: Human Thymus Glands, Young Age, Old Age

INTRODUCTION

Increasingly, the world's population is entering an era in which a larger percentage of people are in their late thirties and forties. People over the age of 60 are expected to account for 25 percent of the entire U.S. population by the year 2050, according to the Census Bureau. Health care costs will rise as more people live longer than previously thought, even as the benefits of longer lives outweigh the drawbacks. With advancing years come immunosenescence, a deterioration of the immune system that results in an increased risk of infection [1, 2], an ineffective immunological response to immunizations [3–5], and a higher incidence of autoimmune disorders and malignancies [6–8]. More than 80 percent of the elderly suffer from at least one chronic disease as a result of diminished immune function, according to the Centers for Disease Control and Prevention (CDC).

Thymus is a major lymphoid organ that produces a wide variety of immunocompetent T cells. Mice thymectomized immediately after birth were found to have underdeveloped lymphoid tissues, sluggish immunological responses, and abnormally high sensitivity to intercurrent infections in 1961 when this was demonstrated (Miller 2002). In a cabin near Pollards Wood in Chalfont St. Giles, roughly an hour's train ride from London, Miller made a significant discovery during his Ph.D. degree. However, the size and function of the thymus declines as we become older. (Gui and colleagues 2012). Naive T cell output decreases with the reduction of Thymus function, which alters the makeup of peripheral T cells and their phenotypic and functionality (Aw and Palmer 2012). Clinical characteristics of immunosenescence may in part be attributed to these alterations (Aw et al. 2007). You need to keep in mind, however, that age-related changes to the thymus are not unique to humans; rather, they are found in many other species that have the thymus (Torroba and Zapata 2003)

While animal studies demonstrate that the release of cells from the thymus is required for the adult preservation of nave peripheral T lymphocytes [9], though thymic activity and naive T cell homeostasis have long been linked, current findings suggest that peripheral proliferation rather than thymic output contributes to the maintenance of naive T cells in young adults. [10] Studies

employing signal-joint T-cell receptor excision circles (sjTREC) have indicated that elderly adults have reduced amounts of mature T-cells.

We conducted present study with aimed to compare the thickness of interlobe connective tissue of human thymus glands and size and number of Hassal's corpuscles between young and old age patients.

MATERIALS AND METHODS

This comparative/observational study was carried out in the Anatomy departments of Jinnah Hospital, Services Hospital, and General Hospital Lahore between November 2013 and October 2014. The participants were all medical students. In this investigation, a total of 54 specimens of human thymus from 70 patients were enlisted as participants. A total of 100 specimens were separated into two groups: Group I has 35 patients under the age of 30 years, and Group II contains 35 patients between the ages of 45 and 60 years.

All specimens of thymus glands from both groups were preserved in 10% formalin solution and then processed for paraffin embedding before being sent to the lab. On a rotary microtome, slices of 5 micron thickness were cut. After that, the sections were deparaffinized and stained with haematologin and easin (H&E) and periodic acid Schiff (PAS) stains, as well as other techniques. The parameters were measured using micrometric techniques. Compare the different parameters between the two groups, such as the thickness of interlobular connective tissue and the thymic capsule, the length of Hassal's corpuscles, and the quantity of them. SPSS 23.0 was used to analyse all of the data. The mean and standard deviation were calculated. The results of the chi-square test were used to compare the findings between the two groups, with a p-value of less than 0.05 considered significant.

RESULTS

In group I, there were 22 patients (62.9 percent) who were male and 13 (37.1 percent) who were female; in group II, there were 21 patients (60 percent) who were male and 14 (40 percent) who were female. The mean age of the patients in group I was 24.16±3.43 years, with a mean BMI of 21.55±6.37 kg/m², and the

mean age of the patients in group II was 52.11±2.887 years, with a mean BMI of 25.07±4.39 kg/m². (table 1)

Table No 1: Demographics of all the patients

Characteristics	Group I	Group II
Gender		
Male	22 (62.9%)	21 (60%)
Female	13 (37.1%)	14 (40%)
Mean age (years)	24.16±3.43	21.55±6.37
Mean BMI (kg/m ²)	52.11±2.87	25.07±4.39

In terms of interlobular connective tissue and thymic capsules, a statistically significant difference was found between groups I and II in both studies. (27.27 ± 7.55 micron vs 51.11±3.37 micron) and (165.17 ±681 micron vs 224.41±4.81 micron) with p-value <0.0001.(table 2)

Table No 2: The thickness of interlobular connective tissue and the thickness of the thymic capsule were compared between the two groups

Variables	Group I	Group II	P-value
Thickness of Interlobular connective tissue	27.27 ± 7.55	51.11±3.37	<0.0001
Thickness of Thymic Capsule	165.17 ±681	224.41± 4.81	<0.0001

Group I showed a statistically significant difference in the size and number of Hassal's corpuscles compared to groups I and II in terms of size and number (108.31±7.67 micron vs 159.19±3.43 micron) and (3.07±0.11 vs 1.01 ± 0.03) with p-value <0.0001.(table 3)

Table No 3: Comparison of size and number of Hassal's corpuscles between both groups

Variables	Group I	Group II	P-value
Size of Hassal's Corpuscles	108.31±7.67	159.19± 3.43	<0.0001
Number of Hassal's Corpuscles	3.07±0.11	1.01 ± 0.03	<0.0001

DISCUSSION

As demonstrated by sjTREC measurements in mice, humans, and other primates, age-related thymic involution is inversely proportional to the decline of thymopoiesis [11]. In humans, females have significantly greater sjTREC levels than age-matched males between the ages of 20 and 60 years old, with the difference remaining significant but becoming less significant after the age of 60 [54]. It is believed that age-related changes in the thymic niches may promote thymic involution because the thymic stroma provides the signals necessary to promote proliferation and differentiation. Cortical and medullary epithelial cells play an important role in this process, with cortical and medullary epithelial cells exerting the greatest influence. As a matter of fact, we have proposed that the extrinsic abnormalities present in the aged microenvironment play a substantial role in the development of age-associated thymic involution. [13,14]

In the current investigation, 70 patients of both sexes were included in the sample. We split all 70 thymus gland specimens into two groups: group I consisted of 22 (62.9 percent) males and 13 (37.1 percent) females, while group II consisted of 21 (60 percent) males and 14 (40 percent) female patients. The mean age of the patients in group I was 24.16±3.43 years, with a mean BMI of 21.55±6.37 kg/m², and the mean age of the patients in group II was 52.11±2.887 years, with a mean BMI of 25.07±4.39 kg/m². Group I consists of 35 patients under the age of 30 years, and group II consists of 35 patients between the ages of 45 and 60 years. We discovered that the colour of the thymus gland in group I had been transformed to the colour of the thymus gland in group II. These findings were consistent with some earlier studies in which the colour of tissues was light and grey in young age and changed to a yellowish brown in old age [15,16], which found that the colour of tissues was pale and grey in young age and changed to a yellowish brown in old age.

A statistically significant difference was found between groups I and II in terms of interlobular connective tissue and thymic capsules (27.27±7.55 micron vs 51.11±3.37 micron) and (165.17±681 micron vs 224.41±4.81 micron) with the significance level set at 0.0001 for both groups I and II. According to our findings, the thickness of the thymic capsule was much less in young patients, while it was rising in older individuals. In the short term, it would appear that the age-associated changes in thymopoiesis are primarily caused by intrinsic defects; however, further investigation reveals that these modifications may be caused in part by extrinsic deficiencies occurring within the aged thymic stromal niche, which result in decreased T cell development. The production of IL-7, which is essential for the process of thymopoiesis, has been found to decrease with age, according to one study. [17,18]

In the present investigation, we discovered a statistically significant difference between groups I and II in terms of the size and number of Hassal's corpuscles (108.31±7.67 micron vs 159.19±3.43 micron) and (3.07±0.11 vs 1.01±0.03), with a p-value less than 0.0001 between the two groups.

Patients of young age had shrinking Hassal's corpuscles but increased numbers, whereas patients of old age had shrinking Hassal's corpuscles but increased numbers, and patients of middle age had shrinking Hassal's corpuscles but increased numbers. These findings were consistent with a number of earlier research in which Hassal's corpuscles in early age were shown to be decreasing in quantity but increasing in size [19,20], among which initially, Hassal observed an increase, which was followed by a drop in the latter portion of his life. Thymus size and function are determined not just by heredity, but also by early childhood nutrition and other stochastic events in the individual's life. Both the pre-natal and early post-natal periods of life are critical for the development of the thymus gland. The long-term consequences of events that occur during these periods may include altered cell-mediated immunity or a quicker thymic maturation in maturity, amongst other consequences. During periods of high sex hormone activity, such as those experienced from adolescence to middle age, the differences between men and women in age-related thymic involution and the ability to produce thymopoiesis are particularly noticeable. When considering prospective techniques to restore thymopoiesis, it is important to analyse their effectiveness in both men and women in order to account for gender differences. Thyroid involution (AIT) is caused by a reduction in the number of thymic stromal cells (TECs) that occurs with age, resulting in a general decline in the quality of the thymic microenvironment. Involution appears to proceed at a steady rate following this rapid early decline, with studies examining the human thymus indicating that 3 percent of thymic tissue is lost per year until middle age, followed by a rate of 1 percent per year [21]. This rate, however, may slow or stop in later life, with studies showing that TREC levels are barely detectable in individuals over the age of 85 years. [21] [22]

CONCLUSION

We found that the thickness of the thymic capsule and interlobular connective tissue decreased dramatically in young patients and increased with age. Also discovered that Hassal's corpuscles grew in quantity and decreased in size in early age, while they grew in size and increased in number in old age. The thymus glands of young and old patients differed significantly in terms of these factors.

REFERENCE

- 1 Yager EJ, Ahmed M, Lanzer K, Randall TD, Woodland DL, Blackman MA. Age-associated decline in T cell repertoire diversity leads to holes in the repertoire and impaired immunity to influenza virus. J Exp Med. 2008;205:711–723.]
- 2 Nikolich-Zugich J. Ageing and life-long maintenance of T-cell subsets in the face of latent persistent infections. Nat Rev Immunol. 2008;8:512–522.

- 3 Haynes L, Swain SL. Why aging T cells fail: implications for vaccination. *Immunity*. 2006;24:663–666.
- 4 Aspinall R, Del Giudice G, Effros RB, Grubeck-Loebenstien B, Sambhara S. Challenges for vaccination in the elderly. *Immun Ageing*. 2007;4:9.
- 5 Cicin-Sain L, Smyk-Pearson S, Currier N, Byrd L, Koudelka C, Robinson T, Swarbrick G, Tackitt S, Legasse A, Fischer M, Nikolich-Zugich D, Park B, Hobbs T, Doane CJ, Mori M, Axthelm MK, Lewinsohn DA, Nikolich-Zugich J. Loss of naive T cells and repertoire constriction predict poor response to vaccination in old primates. *J Immunol*. 2010;184:6739–6745.
- 6 Prelog M. Aging of the immune system: a risk factor for autoimmunity? *Autoimmun Rev*. 2006;5:136–139.
- 7 Fulop T, Kotb R, Fortin CF, Pawelec G, de Angelis F, Larbi A. Potential role of immunosenescence in cancer development. *Ann N Y Acad Sci*. 2010;1197:158–165.
- 8 Foster AD, Sivarapatna A, Gress RE. The aging immune system and its relationship with cancer. *Aging health*. 2011;7:707–718
- 9 Cicin-Sain L, Messaoudi I, Park B, Currier N, Planer S, Fischer M, et al. Dramatic increase in naive T cell turnover is linked to loss of naive T cells from old primates. *Proc Natl Acad Sci U S A* (2007) **104**:19960–5
- 10 Nasi M, Troiano L, Lugli E, Pinti M, Ferraresi R, Monterastelli E, et al. Thymic output and functionality of the IL-7/IL-7 receptor system in centenarians: implications for the neolymphogenesis at the limit of human life. *Aging Cell* (2006) **5**:167–75.
- 11 Mitchell WA, Lang PO, Aspinall R. Tracing thymic output in older individuals. *Clin Exp Immunol*. 2010;161:497–503
- 12 Rezzani R, Nardo L, Favero G, Peroni M, Rodella LF. Thymus and aging: morphological, radiological, and functional overview. *Age (Dordr)*. 2014;36(1):313-351.
- 13 Aw D, Silva AB, Palmer DB. Immunosenescence: emerging challenges for an ageing population. *Immunology* (2007) **120**:435–46
- 14 Aw D, Palmer DB. The origin and implication of thymic involution. *Aging Dis* (2011) **2**:437–43.
- 15 Gui J, Mustachio LM, Su DM, Craig RW. Thymus Size and Age-related Thymic Involution: Early Programming, Sexual Dimorphism, Progenitors and Stroma. *Aging Dis*. 2012;3(3):280-290.
- 16 Van Zant G, Liang Y. Concise review: hematopoietic stem cell aging, life span, and transplantation. *Stem Cells Transl Med* (2012) **9**:651–7
- 17 Hong C, Luckey MA, Park JH. Intrathymic IL-7: the where, when, and why of IL-7 signaling during T cell development. *Semin Immunol* (2012) **24**:151–8. doi:10.1016/j.smim.2012.02.002
- 18 Aspinall R, Andrew D. Thymic atrophy in the mouse is a soluble problem of the thymic environment. *Vaccine* (2000) **18**:1629–37. doi:10.1016/S0264-410X(99)00498-3
- 19 Jeanne B, Ackman, Bojan Kovacina, Brett W. Carter, Carol C. Wu, Amita Sharma, Jo-Anne O. Shepard, Elkan F. Halpern. Sex Difference in Normal Thymic Appearance in Adults 20–30 Years of Age. Jul 1 2013
- 20 Shi X, Zhang P, Sempowski GD, Shellito JE. Thymopoietic and bone marrow response to murine *Pneumocystis pneumonia*. *Infect Immun* (2011) **79**:2031–42
- 21 Ferrando-Martínez S, Ruiz-Mateos E, Hernández A, Gutiérrez E, Rodríguez-Méndez MM, Ordoñez A, et al. Age-related deregulation of naive T cell homeostasis in elderly humans. *Age (Dordr)* (2011) **33**:197–207.
- 22 Mitchell WA, Lang PO, Aspinall R. Tracing thymic output in older individuals. *Clin Exp Immunol* (2010) **161**:497–503.