

Age- And Regional Differences In Human Lymph Node Structure: A Histoarchitectural Analysis Study

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Abstract

Background: Lymph nodes, a component of the lymphatic system are tiny bean-shaped organs. They are variable in number but are constantly found in certain body regions such as the neck, axilla, mediastinum, abdomen, and groin. Many histological changes, like the depletion of germinal centers, and the degree of fibrosis and lipomatosis secondary to the aging process were the main points to be focused on in this study. Recently some clinical procedures like intranodal vaccination, lymph node transplantation, and transfer have demonstrated the need for an accurate knowledge of these degenerative processes.

Objectives: To identify and differentiate the age-related and region-related changes of the histoarchitecture of lymph nodes.

Study Design: A Cross-Sectional study

Place and Duration of Study: The study was conducted at Peshawar Medical College, in collaboration with the Forensic Lab of Khyber Medical College, Peshawar from Jan 2021 to Jun 2021.

Methods: The current study is a cross-sectional study. Which involved 30 autopsies of 3 different age groups. Each group consists of 10 cases. Lymph nodes from different body regions (cervical, axillary, mesenteric, and inguinal regions) were obtained. The deceased adults, who ranged from 15 to 65+ years of age, were included in this study. To evaluate and standardize the degree of degeneration, a scoring system was applied, and the changes were scored as 0 (no change), 1 (mild to moderate change), and 2 (marked change). Data analysis was done using statistical software to compute the prevalence and pattern or variation analysis.

Results: The research examined lymph node modifications in three age groups. The average age of the participants was 55.42 years (± 10.20). The proportion of fibrosis was age-dependent and demonstrated higher frequencies in older ages. The prevalence of lipomatosis rose rapidly with age, affecting a few younger people, and increased significantly by a p-value of 0.0023. Young individuals had more rampant germinal centers with a marked decline in older ones. The depletion of germinal centers was higher with aging ($p=0.0351$, suggesting that there is an age-associated drop in lymph node efficiency).

Conclusion: This study gives us knowledge of some non-pathological changes of lymph nodes with advancing age, and the reason for diminished or weak immunological response to infection and cancer metastasis in the elderly.

Keywords: Lymph node changes, Age-related fibrosis, Lipomatosis, incidence.

Introduction

The lymph node is one of the important organs of the lymphatic system which is composed of lymphatic vessels and lymphoid organs such as the thymus, tonsils, and spleen. These assist in acquired and innate immunity, in filtering and draining the interstitial fluid, and in recycling cells at the end of their life cycle. The fluid that leaks from end-stage capillaries returns to the vascular system via the superficial and deep lymphatic vessels, which in turn drain into the right lymphatic duct and the thoracic duct in the neck. Numerous macrophages cleanse the lymph containing bacteria and other particulate matter; at the same time, these follicles act as sites for local cell-mediated (and humoral) immune responses (1). Lymph nodes are important filtering centers where bacteria and malignant cells that can spread via lymphatics get trapped, taken up by macrophages, and removed. Lymphatic vessels are the routes by which lymphocytes, monocytes, and plasma cells circulate between blood (esp. through

bone marrow) and lysosomes: i.e., high concentration of antibodies making cellulose flower-like. Such methods as lymph node transplantation to improve post-operative metastasis filtration [2], or the improvement of lymph transport and resorption after regeneration of fragments in acquired lymphedema (3,4,5) are some recent advances. An alternative method for immediate desensitization is intranodal vaccination (7,8,9,10). This study aimed at grading lymph node degeneration by using the density of fibrosis, lipomatosis, and germinal centers depleted as fields to score them save on microscopic data for a factual determination. The findings established in this study will add to the current literature on degenerative changes of lymph nodes and enable us to set intervention measures appropriately for the early diagnosis, prognosis as well as therapy regarding infectious or malignant conditions.

Methods

Samples were obtained from cadavers with times elapsing between death and specimen collection no later than 04 hours, in different settings in the Forensic Medicine Department of Khyber Medical College (KMC) Peshawar, KPK. The rest of the study was carried out in the Anatomy and Pathology Departments of Peshawar Medical College (PMC) Peshawar. This study used a convenience sample of Pakistani adult men and women from young adults to 65 and above years of age, with no significant history of any chronic illness or malignancy. A total number of 30 autopsies were included in this study. The deceased adults ranging from 15 to 65+ years of age making a mean age of 36 ± 15.7 years were included in this study and were grouped according to WHO classification into three groups:

- Group A comprises younger adults of 15-24 years of age.
- Group B comprises the middle adults 25-44 years of age.
- Group C comprises older adults 45-65+ years of age.

After obtaining consent by the attendant samples were collected from different regions of the same deceased. The incisions were made on the appropriate site and after careful dissection; lymph nodes were excised and were put and fixed in the 10% solution of NBF for preservation. After dehydration, specimens were embedded in fresh paraffin, Sections were cut using a microtome. paraffin block was serially cut to 5- μ m thickness. 5 slides of each specimen were prepared in serial order. The sections were stained with H& E method, for routine histological studies, and Masson Trichrome for observing fibrosis.

Histological Examination

The following observations were made:

- Germinal center 10x
- Degree of fibrosis 10x
- Degree of lipomatosis 10x

To evaluate and standardize the degree of degeneration, a scoring system was applied, and the changes were scored as 0 (no change), 1 (mild to moderate change), and 2 (marked change).

Data collection:

Tissue samples from lymph node biopsies were analyzed in different age cohorts to collect and extract data. Results: All biopsies were reviewed for fibrosis, lipomatosis, and the presence of germinal centers. Histopathological results were registered and statistically analyzed. All the demographics like age, sex, and mean age were noted. Statistical tests were used to determine significance by correlating the results with age.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 17. Statistical results were given as mean and standard deviation for continuous variables. Frequencies and percentages were calculated for categorical variables. Fisher's exact test was applied to observe an association between categorical variables, a p-value of ≤ 0.05 was considered as statistically significant.

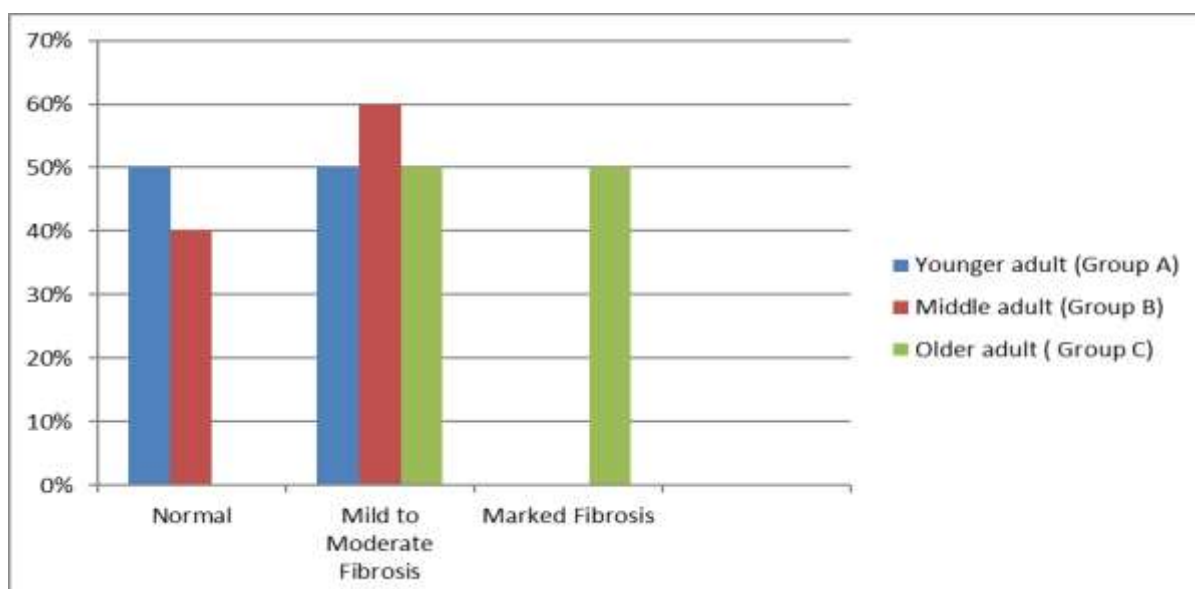
Results

Fibrosis was found to be one of the most common findings associated with aging. It was recorded in 21 out of 30 (70%) cases. Based on several observations, 5/10 nodes of group A individuals were presented with a mild to moderate degree of fibrosis, while the rest of the nodes did not reveal any fibrosis. In group B, the degree of fibrosis was different, as 4 out of 10 cases didn't show any fibrosis, however, 6/10 nodes were categorized with

mild to moderate degree of fibrosis. In summary, the analysis of the degree of fibrosis revealed a high prevalence in group C individuals, accounting for 47.6% of total cases. Thus, our results suggest a possible link between aging and fibrosis, and this has been confirmed by statistical analysis with a highly significant p-value of 0.0042.

The degree of fibrosis is recorded in Table 1 and Bar chart-I.

Degree of Fibrosis	Age groups			Frequency	percent
	Younger adult (A)	Middle adult (B)	Older adult (C)		
Normal	5	4	0	9	30.0
Mild to moderate loss	5	6	5	16	53.3
Marked loss	0	0	5	5	16.7
Total	10	10	10	30	100



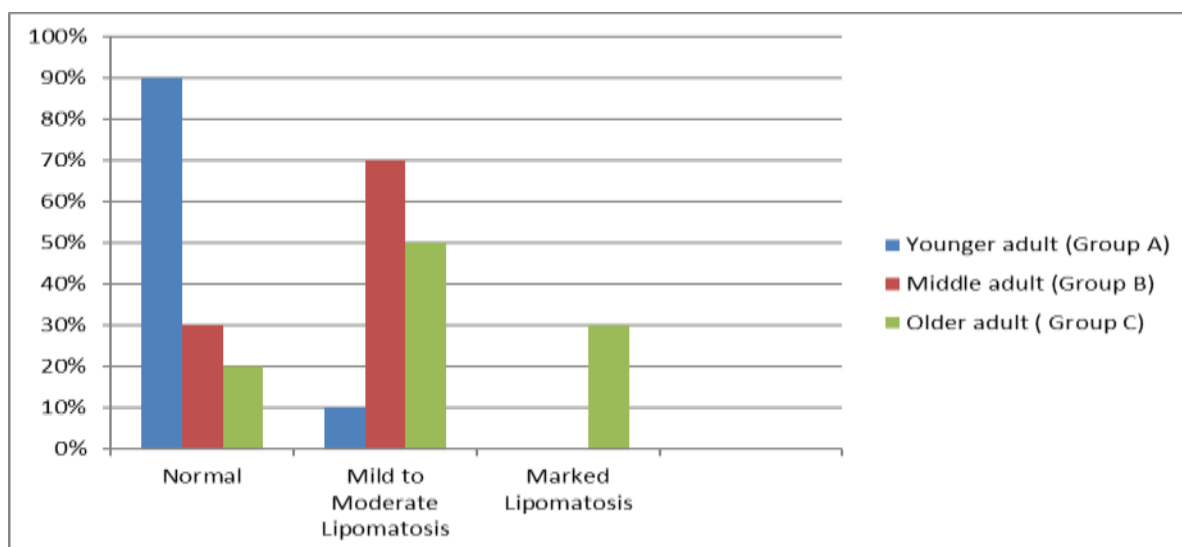
Column –I, shows the degree of Fibrosis in 3 different age groups

Lipomatosis

Group A, lipomatosis was rarely seen i.e., only a single case (1/10) displayed mild to moderate degree. In the group B individuals, however, its occurrence was constant, with mild to moderate lipomatosis in 7 out of 10 lymph nodes, while the rest of the nodes showed no change. Lipomatosis and its extent were marked in group C, whereas mild to moderate change was noted in 5 (50%) nodes, and 3 (30%) lymph nodes were markedly affected. However, no fatty deposits could be seen in the remaining 20% of lymph nodes. Thus, our result suggests a possible relation between aging and lipomatosis, and this has been confirmed by statistical analysis with a highly significant p-value of 0.0023.

The degree of lipomatosis is recorded in Table 2 and Bar chart-II.

Degree of Lipomatosis	Age groups			Frequency	percent
	Younger adult (A)	Middle adult (B)	Older adult (C)		
Normal	9	3	2	14	46.7
Mild to moderate loss	1	7	5	13	43.3
Marked loss	0	0	3	3	10.0
Total	10	10	10	30	100



Column II shows the degree of lipomatosis in 3 different age groups

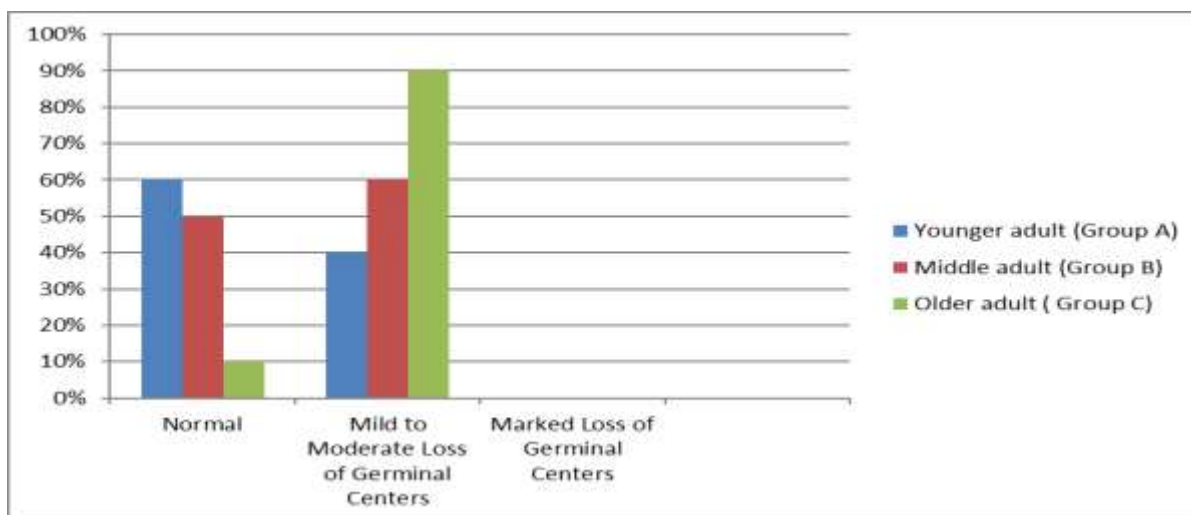
Germinal Centers

Prominent germinal centers were found in 40% of the nodes. Group A showed the highest incidence (60%), whereas Group C showed the lowest i.e. 10%, while in Group B, 40% of the individuals revealed prominent germinal centers. Mild to moderate loss of germinal centers was noted almost evenly in all 3 age groups, being highly significant in group C involving almost 60 % of the adults; however, 20 % of group B also exhibited mild to moderate loss, whereas none of the group A showed any evidence of loss. Marked loss of germinal centers was not observed in any of the individuals of the 3 groups. Thus, our results demonstrate a possible association between aging and loss of germinal centers, and this has been confirmed by statistical analysis with a highly significant p-value of 0.0351.

Degree Of Loss of Germinal Centers

Degree of loss of Germinal Centers	Age groups			Frequency	percent
	Younger adult (A)	Middle adult (B)	Older adult (C)		
Normal	6	5	1	12	40.0
Mild to moderate loss	4	5	9	18	60.3
Marked loss	0	0	0	0	00.0
Total	10	10	10	30	100

Degree Of Loss Of Germinal Centers



Column v shows the degree of germinal center loss in 3 different age groups

Discussion

The presence and extent of fibrosis in our study suggest an association between age and degree of fibrosis, as all individuals over 65 years demonstrated some level of interstitial or pleural lung disease. Our results for fibrosis prevailed in similar age groups to a study by Catarina Hadamitzky et al. (11):2010 regular, healthy inguinal lymph nodes without malignancy or infectious illness in different age groups. It gave them a high prevalence of fibrosis in the 61-75 and 76+ age groups with widely different severity. Notably, a subset of lymph nodes from the 16-30-year-olds were presented with mild to severe fibrosis as well. Lymph node fibrosis was mild to moderate in most of the lymph nodes from age group 31-45 and 46-60 demonstrating that Fibrosis with Lymph Nodes is not only an issue for people in older groups, but also affects young adults as well as adults (12). These observations are consistent with the results of a study by Catarina Hadamitzky and colleagues [22]. (2010)(13). They found that lipomatosis was hardly ever observed in people ages 16-30, but became more common with age: distances from age groups where mild lipomatosis occurred were two of the lymph nodes studied among those over ages 31 to <45; four nodes among subjects aged ≥ 46 to <60 years; four carriers examined from within carrier carrying/community under between contributors aged >61 and ≤ 75 years-old whole-family on both sides as opposed high-rate as compared state/establishment happens three-area-treated youth being-cared-for displayed for each-viewed happenings. As a result, there is an increase in lymph node atrophy with age as seen from the analysis (14). In summary, our results are histologically and statistically meaningful concerning aging and lipomatosis. This study is also consistent with the results of Luscieti P et al. (1980) (15). P. Luscieti et al. defined the germinal centers which were absent in lymph nodes from premature infants and a young un-lifted newborn infant, appeared during the first year of life, reached maximal numbers at childhood to younger adult age levels, then wined and declined in old age (16).

Conclusion Human Lymph node degeneration is widespread and strong in older age. Depending on the degree of degeneration, they are used for interventions like lymph node transfer and transplantation still in prototype or allergen desensitization. Furthermore, both age- as well as regional differences are important considerations for lymph node biology to make any sense in terms of its morphological and functional standpoint.

Limitations:

The small sample size may limit the generalizability of our findings. A limitation of the cross-sectional design is that we are unable to infer causality from age on these changes in lymph nodes. Moreover, the study was not designed to control confounding factors like comorbidities and medications that may alter lymph node histopathology, which could have played a role in biasing results.

Future Findings:

For any future study, it is recommended that: Capsular, Cortical, and medullary thickness should be measured for further confirmation of senile involution effects on lymph nodes having a good number of specimens based on which standard criteria can be established.

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Conflict of Interest: There is no conflict of interest.

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study. Shamilah Hafizi

Drafting: Farooq Khan

Data Analysis: Rifat Shamim

Critical Review; Zafar Iqbal

Final Approval of version: Nighat Ara

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