

## Follicles in Hypertrophied Tonsils

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### ABSTRACT

**Aim:** To study histomorphological changes of lymphoid follicles and to co-relate the extent of these changes to the tonsillar hypertrophy.

**Methods:** Enlarged tonsils from thirty children with obstructive airway symptoms were obtained after tonsillectomy. Normal tonsils were obtained from 10 children's at autopsy.

**Results:** In hypertrophied tonsils size, weight, epithelium and lymphoid compartment, all were affected. It was observed that there was increase in size of germinal centers, decrease in no of lymphoid follicles due to increase in size but overall no remains the same.

**Conclusion:** Hypertrophic changes are probably immunological response to exposure to different antigens in an exaggerated manner manifested by histological changes.

**Keywords:** Hypertrophied tonsils, lymphoid follicles, polarity

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### INTRODUCTION

Tonsillar hypertrophy and its complications are primary causes of tonsillectomy<sup>1</sup>. Tonsillar hypertrophy was observed in 11% school children in Turkey and adenotonsillar hypertrophy was observed 55.3% in school going children in Brazil<sup>2,3</sup>.

Generally tonsils start to hypertrophy or increase in size within the first three years of life, which is the period of highest immunological activity during childhood<sup>4</sup>. The palatine tonsils increase in size throughout childhood and tend to regress or involute at puberty, when the reactive lymphoid tissue begins to atrophy<sup>5,6</sup>. This hypertrophy is not a disease but is due to increased immunological activity and is clinically known as tonsillar hypertrophy<sup>5</sup>. In physiological hypertrophy, tonsils increase in size and weight with absence of both visible congestion on anterior pillars and cheesy discharge on pressing. Tonsillar crypts contain dead and alive lymphocytes, desquamated epithelial cells and bacteria more than the normal tonsils<sup>7</sup>. Sometimes this increase is very rapid and develops serious symptoms and complications<sup>8</sup>. It is no doubt that if there is moderate hypertrophy of the lymphoid tissue of the pharynx, it will cause an obstruction of this part of the airway and may alter the mode of breathing, hinder speech and swallowing and disturb sleep<sup>9</sup>.

According to some researches interfollicular area is reduced because of the enlarged lymphoid follicles in tonsillar hypertrophy and it is relatively increased in diseased tonsils<sup>5,10</sup>. Similarly when the T-lymphocytes are activated, they enlarge to form immunoblasts. Histologically they are similar to their B-cells counterparts. In T-cell dominated

immunological response, the interfollicular area may be greatly expanded. Activated T-lymphocytes are disseminated via the circulation to distant sites, where much of their activity occurs<sup>11</sup>. While others stated that the interfollicular area remains unaffected<sup>12</sup>.

Epithelium of human palatine tonsil consists of 2 different compartments i.e., surface epithelium and crypt epithelium. The epithelium of tonsils is characterized as lymphoepithelium<sup>5,13</sup>. The epithelial area which is exposed to antigen is increased by 10 to 30 blind-ending crypts, and extends deeply into the tonsillar tissue<sup>14</sup>. The lymphoid tissue, which contains predominantly IgD and IgA producing B lymphocytes (including some mature plasma cells), T lymphocytes and antigen presenting cells<sup>15</sup>. The lymphoid tissue of the tonsils is directly exposed to the outside environment through inspired air or by ingested food. Electron microscopic observations have demonstrated that the mature crypt epithelium is porous and allows the protrusion of lymphocytes through these pores that mediate the immune response<sup>21</sup>. It explains the functions of the palatine tonsils i.e. they sample the environmental antigens (which were inhaled or ingested) and participate in the initiation and maintenance of the local and systemic immune responses<sup>16</sup>.

Hypertrophied tonsils are characterized by enlarged lymphoid follicles with significant enlargement of germinal centers. The germinal centre is pale but not of uniform colour. It is darker towards the medulla, indicating the organization of the different types of the cells within it. These cells include the B-lymphocytes in their different stages of maturity. Mitotic figures of B cells indicate a hyperplastic condition of B lymphocytes in the germinal centres<sup>7,11</sup>. In addition to these B-

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lymphocytes follicular dendritic cells (the major antigen presenting cells of the follicles) and the tingible body macrophages are also present in the germinal centers. Tingible bodies are the macrophages which have phagocytosed the surrounding immature B-lymphocytes which were not effective in generating a high affinity antibody<sup>11</sup>. There is also sharp demarcation of germinal centers from mantle zone lymphocytes because in the mantle zone B-lymphocytes are arranged circumferentially with an onion skin pattern, and are of small sized and closely packed<sup>17</sup>.

Although the exact pathophysiological mechanisms of lymphoid tissue hypertrophy of upper airway are not known. There is one possibility that during early postnatal life, respiratory viruses may modify the neuroimmunomodulatory networks within the tonsils, and in response to various exogenous stimuli promote different patterns of proliferation<sup>18</sup>.

H influenza is the bacterium most often isolated in hypertrophied tonsils others being alpha and beta haemolytic streptococcal species, staphylococcus aureus, and bacteroids<sup>19</sup>.

Previous works by researchers have shown increased release of potent proinflammatory mediators, such as TNF-alpha, IL-6, IL-8 and other cytokines are responsible for both the local and systemic inflammatory processes elicited by the presence of upper airway obstruction. These cytokines will result in the recruitment of lymphocytes and macrophages which in turn play a vital role in the host immune response to inflammation and infection<sup>20</sup>.

By comparing with recurrent infection this local inflammation is enhanced in obstructive sleep apnea. In this context, it can be speculated that in the patients with OSA concentrations of cytokines are elevated as compared to respiratory infection. This may reciprocally reflect that in OSA there is more pronounced cell proliferative processes<sup>20</sup>. Abnormal nocturnal growth hormone secretion and impaired growth hormone action results from the abnormal sleep pattern. Since growth hormone is to be released while sleeping and obstructive tonsillar hypertrophy (OTH) is related with disturbed sleep. Retardation of growth in OTH may be the result of suppressed plasma ghrelin and serum insulin like growth factor-1 (IGF-1). Ghrelin is a peptide hormone, which stimulates secretion of growth hormone. Ghrelin is secreted from the placenta in the fetus and from the stomach and intestines in post natal life, and then transferred to the target tissues via blood<sup>21</sup>.

Research related with the comparison of histological changes in chronic tonsillitis and tonsillar hypertrophy, especially in the lymphoid follicles was

carried out in 2003 by Pang and Wang. They found that histologically an enlargement of lymphoid follicles is characteristic of tonsillar hypertrophy when compared with recurrent tonsillitis, indicating a hyperplastic condition of lymphoid cells in the germinal centres<sup>22</sup>.

An equally reliable and useful feature that aids in differentiating tonsillar hyperplasia is the polarity of lymphoid follicles. Polarity is the mantle zone hyperplasia localized at one pole and is towards the antigenic stimulation. However polarization of follicles is not always present in follicular hyperplasia and if found may be confined to a minority of germinal centers i.e. polarization of large transformed cells in germinal centers. However whenever it is present, it is a feature of reactive hyperplasia<sup>24</sup>. Although there is variation in the size and shape of germinal centers, there is preservation of tonsillar architecture<sup>23</sup>.

## MATERIALS AND METHODS

It was a descriptive study and conducted in the Department of Anatomy, King Edward Medical University, Lahore. Non hypertrophic tonsils from autopsies of ten children were collected from Department of Forensic Medicine, King Edward Medical University, Lahore. These were categorized as Group A (control group).

Thirty samples were collected from children who were diagnosed with obstructive tonsillar hypertrophy (after a detailed history taken on a proforma). They underwent tonsillectomy at the Department of ENT Unit-II Mayo Hospital, Lahore (15 children), Department of ENT Services Hospital Lahore (6 children) and Department of ENT Sir Ganga Ram Hospital Lahore (9 children). These were categorized as Group B. Prior to autopsy or surgery a written informed consent was obtained from the guardians or parents.

For the children undergoing tonsillectomies for hypertrophied tonsils, age range was 4-10 years (male and female children), with history of obstructive symptoms were included in the study. For autopsies dead bodies of children both male and female of age 4-10 years received within 12 hours of death.

Data were entered and analyzed using SPSS 13 version. All qualitative data was presented in form of multiple bar charts with respect to study groups. Quantitative data was presented in the form of mean  $\pm$  S.D along with its minimum and maximum value. Chi-square test of association was used for the comparison of qualitative data in all study groups. Mann-Whitney U Test was applied for the comparison of quantitative data in both study groups. A p-value less or equal to 0.05 was taken as significant.

**RESULTS**

It was observed that there was no visible congestion, ulceration or pustule on hypertrophied tonsils. The mean weight of tonsils from group A was  $1.42 \pm 0.19$  gm. The mean weight of tonsils from group B was  $3.41 \pm 0.43$  gm (Table 1). Like weight, size of hypertrophied tonsils was also increased as shown in table 2. Polarity of lymphoid follicles is a feature of reactive hyperplasia and is absent in the normal tonsils. Polarity was seen in 21(70%) cases in group B, while it was absent in 9(30%) cases.  $p$ -value = 0.000 (Fig 1, 2). Number of lymphoid follicles was also increased in hypertrophied group. The average number of lymphoid follicles in group A was  $5 \pm 0.94$ /LPF and it was  $2.11 \pm 0.90$ /LPF in group B (fig 3). There was increase in size of germinal centre in group B as compared to group A as shown in fig 4.

Table 1: Weight of tonsils in study groups

	Weight (gm)	
	Group A	Group B
N	10	30
Mean	1.42	3.41
Std. Deviation	0.19	0.43
Std. Error	0.06	0.08
Minimum	1.15	2.54
Maximum	1.65	4.12

$P$ -value = 0.000 (significant)

Table 2: Size of tonsils in study groups

	Size (cm <sup>3</sup> )	
	Group A	Group B
N	10	30
Mean	3.63	8.20
Std. Deviation	2.13	4.83
Std. Error	0.67	0.88
Minimum	1.80	3.90
Maximum	7.50	19.40

$p$ -value = 0.007 (significant)

Fig.1: A photomicrograph of the lymphoid follicle from group B tonsil showing polarity (yellow arrow).

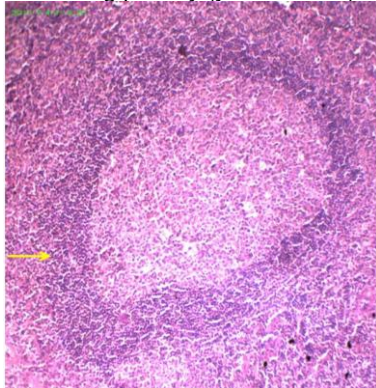


Fig. 2: A photomicrograph of the lymphoid follicle from group A and B showing absence and presence of polarity of lymphoid follicle. Yellow arrow showing polarity.

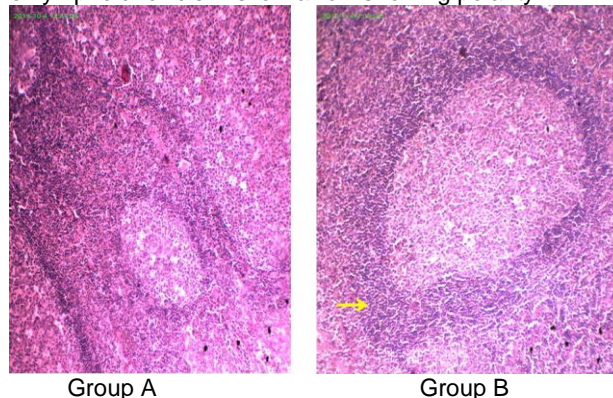


Fig. 3: A Photomicrograph of the group A (control group) and group B showing comparison of the number of lymphoid follicles/LPF.

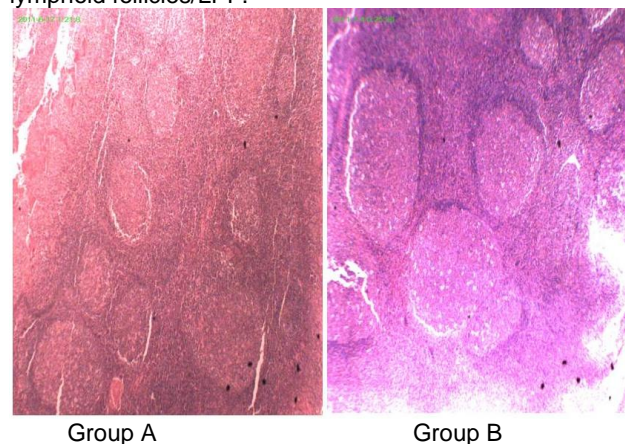
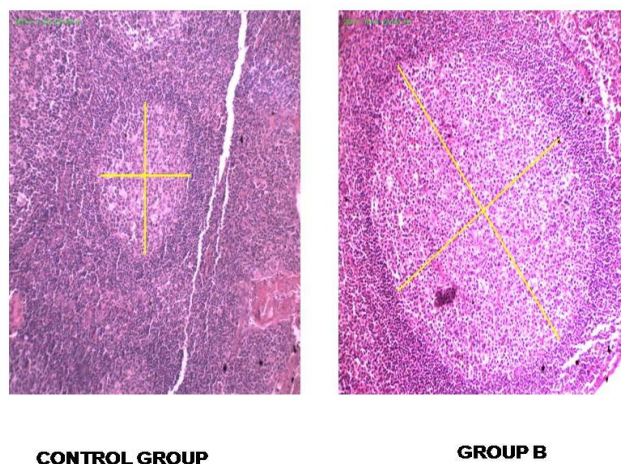


Fig. 4: A photomicrograph of two groups comparing the size of the germinal centers of the groups A and B



In this study normal tonsils (Group A) were compared with hypertrophied tonsils (Group B)

in children of 4-10 years of age. It was observed that there was no change in colour and absence of congestion, no pustules and ulcer formation on the hypertrophied tonsils. However the weight and size of the tonsils were significantly increased in group B as compared with group A (Tables 1, 2).

Polarity of lymphoid follicles is a feature of reactive hyperplasia. Polarity is defined as the mantle zone hyperplasia localized at one pole and is towards the antigenic stimulation to clear the bacteria or pathogen. Polarity of the follicles was found in 21(70%) cases in group B (Fig. 1) while it was absent in rest of 9(30%) cases. Polarity was not present in the normal tissue (Fig. 2). This finding was consistent with the criteria laid down in the classic article by Rappaport et al., and further developed by Nathwani et al., to distinguish the reactive follicular hyperplasia from follicular lymphoma. Nathwani et al found polarity of lymphoid follicles in 7 out of 20 i.e. 35% of specimens. According to them, reactive follicles vary considerably in size and shape; their margins are sharply defined and surrounded by a mantle of small lymphocytes often arranged circumferentially and sometimes concentrating on one pole of the follicle (polarity)<sup>24,25</sup>.

## CONCLUSION

Immunopathogenesis of tonsillar hypertrophy is, at least partly, related to some latent bacterial infection<sup>26</sup>. Probably this latent low dose continuous bacterial stimulation was the cause of tonsillar hypertrophy and hyperplasia. Immunomodulation is required in the form of some vaccine or drug to control hypertrophy and hyperplasia of tonsils.

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