**Localization of tongue lesions according to subsites: bad and better neighborhoods**

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**Abstract**

**Objective:** Tongue lesions constitute a considerable proportion of oral mucosal pathologies. Those lesions appear upon the different subsites of the tongue: the dorsal, ventral, lateral, and tip and may be either reactive, infectious, immunologic, or neoplastic. The aim of our study was to analyze the potential differences between these subsites regarding the types of lesions and the clinicopathological concordance.

**Materials and Methods**: Retrospective analysis of human tongue lesions, diagnosed over a period of 7 years (2016-2022) in our institution. The tongue was divided into subsites (lateral, dorsal, ventral and tip of tongue), and diagnoses were classified into different categories.

**Results**: The lateral aspect of the tongue was the most affected site (43.6%). Most of the lesions (64.8%) were classified as reactive, infectious and tumor like lesions. More malignant or premalignant lesions were found on the lateral aspect (31%) compared to the other aspects, and almost all lesions observed on the tip of the tongue (96%) were reactive, infectious, or tumor-like lesions. The clinical diagnosis concurred with the histopathological diagnosis in only (62.3%) of cases on the lateral aspect, compared to 92.6% concordance at the tip of tongue.

**Conclusions**: The findings support the tongue may be perceived as a diverse organ composed of better and worse neighborhoods both in terms of the types of lesions and in regard to the clinico-pathologic concordance. These findings should be further supported by preclinical studies focusing on microenvironmental properties of the different subsites of the tongue.

**Keywords:** tongue, subsites, biopsy, clinicopathological, neighbourhood

**Introduction**

The human tongue is a mainly muscular unique organ, involved in important functions of the oral mucosa including tasting, phonation, mastication, deglutition, maintenance of oral hygiene, protection of deeper structures, and facilitation of orofacial growth1. The easy clinical accessibility of the tongue makes it a good health indicator for clinical examinations2. The condition of the tongue has been considered a reflection of local and systemic diseases, such as candidiasis, anemia, endocrine disorders, metabolic diseases, storage diseases and neurologic deficits3,4. While certain diagnoses can be made on bases of clinical appearance, the tongue may, on occasion, be affected by pathologic conditions that necessitate a biopsy and a consequent histopathlogical diagnosis5.

Epidemiological studies have shown that tongue lesions constitute a considerable proportion of oral mucosal lesions and that prevalence rates vary in different parts of the world6 .Variation in prevalence rates indicate a lack of consistency in the data for reference3. Those lesions might be either reactive, arising in response to local trauma (e.g., irritation fibroma, pyogenic granuloma, mucocele), inflammatory or immunologic (e.g., lichen planus, lichenoid reaction), or neoplastic that can be either benign (e.g., lipoma, schwannoma) or malignant (e.g., squamous cell carcinoma, sarcoma) 7.

The tongue encompasses of the dorsal, lateral, ventral aspects and tip of tongue. Little is known about the distribution of lesions according to these tongue subsites. It is well known, for example, that oral squamous cell carcinoma is more prevalent on the lateral aspect of the tongue4, and relatively rare on the dorsal aspect9 .

The present study was conducted with special focus on the different subsites of the human tongue. The purpose of the study was to view the tongue as a whole, in comparison to its different subsites. Specifically, we aimed at analyzing the potential differences between these subsites regarding the types of lesions and the clinicopathological concordance, a finding that could potentially enhance the clinical accuracy in diagnosing tongue lesions.

**Materials and Methods**

The study was approved by the Institutional Review Board IRB (#0011-22) and conducted as a retrospective analysis of human tongue lesions, diagnosed over a period of 7 years (2016-2022) in the institute of Pathology of our institution. We included all the diagnostic biopsies records from the tongue, studied the medical files of the patients and collected the following relevant data: Demographic information: age and gender, involved aspect of tongue (lateral, dorsal, ventral and tip of tongue), histopathological diagnosis, and pre-biopsy clinical differential diagnosis. The collected data was summarized, and the clinical and histopathological diagnoses were classified into one of the following categories: Reactive, infectious and tumor like lesions, Benign Lesions, Immune/Autoimmune lesions, Lichenoid and undetermined significance lesions, Premalignant Lesions, and Malignant Lesions (Table 1).

Statistical analysis of the results was carried out by biostatistics experts’ authors ARB + NLZ by the R statistical software27. Lesion types and tongue aspects were described by counts and percentages. Regarding the clinicopathological concordance, when the pre-biopsy clinical diagnosis and histopathological diagnosis were classified in the same lesion type category, it was considered a “match”. The categories were further divided into two groups for the purpose of comparing the clinicopathological match rates between them: the first included the malignant and premalignant lesions, while the second group included the remaining categories (non-malignant or premalignant lesions). Fisher’s test was used for comparing the distributions of tongue aspects between lesion types and for comparing clinicopathological match rates between tongue aspects, across different types of diagnosis. P-values less than 0.05 were considered significant.

**Results**

During the years 2016-2022, there were 3536 biopsies from the oral cavity performed over the study period in the institute of Pathology of the Barzilai University Medical Center, 383 cases (10.8%) were tongue biopsies from 174 (45.4%) males and 209 (54.6%) females, constituting a male to female ratio of 1:1.2. The age range of the patients was 5-99 years with a mean age of 52±21.7 years.

The majority of the histologically observed lesions (64.8%) were reactive, infectious, or tumor-like lesions, while 14.8% were malignant and premalignant (Figure 1).

Most of the tongue lesions were encountered at the lateral aspect of the tongue (43.6%)

followed by dorsal (26.4%), tip (19.1%) and ventral aspect (8.6%) respectively (Table 2, Figure 2).

***Tongue lesions according to subsites***

**Lateral aspect**: lesions observed on the lateral aspect of the tongue in descending order were (44%) reactive, infectious and tumor like lesions, (21.1%) malignant, (16.3%) lichenoid and undetermined significance, (10.2%) premalignant, (4.8%) immune/autoimmune lesions and (3.6%) benign lesions (Table 5, Figure 3). The clinical diagnosis “matched” the histopathological result in only 62.3% of cases (Table 6).

**Dorsal aspect:** lesions on the dorsal aspect of the tongue in descending order were (72.3%) reactive, infectious and tumor like, (12.9%) benign, (11.9%) lichenoid and undetermined significance, (3%) malignant, no premalignant lesions and no immune/autoimmune lesions were encountered (Table 5, Figure 3). The clinical diagnosis “matched” the histopathological result in 73.1% of cases (Table 6).

**Ventral aspect**: lesions on the ventral aspect of the tongue in descending order were (72.7%) reactive, infectious and tumor like, (18.2%) lichenoid and undetermined significance, (6.1%) immune/autoimmune, (3%) malignant lesions, no benign lesions, and no premalignant lesions (Table 5, Figure 3). The clinical diagnosis “matched” the histopathological result in 76.7% of the cases (Table 6).

**Tip of tongue:** lesions on the tip of the tongue were almost always (95.9%) reactive, infectious and tumor like, (1.4%) lichenoid and undetermined significance, (1.4%) malignant, (1.4%) benign lesions, (Table 5, figure 3). The clinical diagnosis “matched” the histopathological result in 92.6% of cases (Table 6).

Regarding the clinicopathological concordance and the differences in match rates, generally the pre-biopsy clinical diagnosis matched the histopathological diagnosis and was correctly classified in the same category for 252 (65.8%) of total cases. In the group of malignant or premalignant lesions, only 31 (52.5%) cases matched, while for the second group which included the remaining categories, 221 (76%) cases matched. In terms of the differences in match rate according to subsites (neighborhoods), the match rate in the tip of the tongue was the highest 92.6%, while the match rate in the lateral aspect was the lowest 62.3%.

***Tongue lesions according to age***

Thirty-two cases (8.3%) occurred in pediatric patients aged 18 and below. In those, the most affected subsite was the ventral aspect (37.4%) and the most prevalent category (78.12%) was reactive, infectious and tumor like lesions (Table 3). 160 cases (41.7%) were found in the elderly (aged 60 and above), where the most affected subsite was the lateral aspect (62.5%), and the most prevalent category (43.1%) was reactive, infectious and tumor like lesions (Table 4). It should be noted that while the lateral aspect was the most affected subsite in the elderly group patients’ it was the least affected in the pediatric patient’s group (3%), and while the ventral aspect was the most affected subsite in pediatric patients’ group it was the least affected subsite in the elderly group of patients (7%). Reactive, infectious and tumor like lesions were the most prevalent category across all age groups. The elderly patient group exhibited the highest proportion of malignant and premalignant lesions (28.75%).

**Discussion**

As far as we are aware, this is the first study to examine the prevalence and clinicopathological correlations of tongue lesions focusing on the different subsites of the tongue.

Tongue lesions constituted an appreciable percentage (10.8%) of all histologically diagnosed cases of oral cavity biopsies in our institution, which is higher than 4-9.2 % reported by some authors  10,11,12,13,14 , and lower than the 18.52–52.3% reported by some other authors15,6,16,17,18 for the majority of clinical studies.The prevalence of tongue lesions in the clinical studies may be higher than in the present study since lesions diagnoses such as geographic tongue, coated or fissured tongue can be made on bases of clinical appearance and are not usually submitted to histopathological examination.

In the present study and in accordance with the studies by Costa et al.2 Gambino et al.8 and Miyake et al.19, reactive, infectious, or tumor-like lesions were the most diagnosed tongue lesions. And unlike the study by Alaeddini et al12, where tongue lesions were primarily classified into the immune-mediated group and the reactive/inflammatory category, respectively. Moreover, according to our analysis reactive, infectious, or tumor-like lesions category was the most prevalent category across all subsites. The mean age of the patients in the present study was 52 years, which is comparable to 45-48 reported by Lasisi et al.10, Dhanuthai et al.14, Shamloo et al.11, and Alaeddini et al.12.

Most of the tongue lesions were encountered on the lateral aspect of the tongue (43.6%), which is in accordance with the studies by Aittiwarapoj et al.20 Shamloo et al.11 Gambino et al8 and Miyake et al18. However, studies by Lasisi et al.10 and Alaeddini et al.12 found the dorsum of the tongue followed by lateral aspect was the most affected subsite.

In the present study, types of lesions varied in distribution between the different subsites. More malignant/premalignant cases were diagnosed on the lateral aspect (31%), compared to the other aspects, and almost all lesions observed at the tip of the tongue (96%), were reactive, infectious or tumor-like lesions. Upon these finding the tip of the tongue could be considered the best neighborhood of the tongue from the patients’ point of view, and the lateral aspect the worst.

The match between the clinical and histopathological diagnosis was also best achieved on the tip of the tongue, making it the best neighborhood from the clinician's perspective as well, followed by ventral, dorsal and finally lateral aspect that could be considered the worst neighborhood from that aspect as well. The differences in match rates between the clinical and histopathological diagnosis emphasize the importance of the histopathologic analysis in the final diagnosis particularly on the lateral aspect.

When considering the pre-biopsy evaluation and clinicopathological correlation, the clinical diagnosis was correctly classified in the same category as the histopathological result for 252 (65.8%) of all cases. For malignant or premalignant clinical diagnosis, the accuracy was significantly lower with only 31 (52.5%) cases matched, while for other diagnoses, 221 (76%) matched. This demonstrates the fact that the clinical ability to assess the neoplastic lesion is relatively limited.

When examining the incidence and distribution of tongue lesions according to age, the results show that reactive and benign tongue lesions mostly affected younger age groups in the ventral aspect, whereas malignant and premalignant tongue lesions affected older age groups and lateral aspect was the most affected subsite. This finding suggests that advancing age is a significant risk factor for cancer.

The differences between the subsites of the tongue may be attributed to extrinsic factors such as oral habits or to intrinsic factors such as cell population. In a recent study, Lyras et al.21 discussed the composition and the transcriptional landscape of the tongue immune system and succeeded to identify distinct local immune cell populations and described two specific subsets of tongue-resident macrophages occupying discrete anatomical niches. Further studies are needed to determine whether the differences among the different subsites can be attributed to differences in the microenvironmental niches that contain different subpopulations of fibroblastic or immunologic cells.

In conclusion, different subsites of the tongue do not behave in the same manner, thus constitute different neighborhoods: worse and better. Both from the patient and clinicians’ perspective, the best neighborhood is the tip of the tongue, and worst is the lateral aspect. This study provides a novel point of view by demonstrating the differences throughout the different subsites of the tongue in terms of types of lesions and clinicopathological concordance.

**Tables, figures and Figure Legends**

**Table 1.** Age, gender, and location of tongue lesions according to type of lesion categories

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Serial No. | Age | Gender | Pre- biopsy Clinical diagnosis | Type of lesion  (According to clinical diagnosis) | Histopathological diagnosis | Type of lesion  (According to Histopathological diagnosis) | Involved aspect of tongue | Clinic histopathological correlation |

\*Type of lesion: **A**. Reactive, infectious and tumor like lesions, **B**. Lichenoid and undetermined significance lesions, **C**. Benign Lesions, **D**. Malignant Lesions, **E**. Premalignant Lesions and **F**. Immune/Autoimmune lesions

**Table 2.** Distribution of tongue lesions according to subsites

|  |  |  |
| --- | --- | --- |
| category | n | % |
| **Dorsal Aspect** | 101 | 26.4% |
| **Lateral Aspect** | 167 | 43.6% |
| **Tip Of Tongue** | 73 | 19.1% |
| **Ventral Aspect** | 33 | 8.6% |
| <NA> | 9 | 2.3% |
| Total | 383 | 100% |

**Table 3.** Distribution of tongue lesions according to categories and subsites in pediatric patients (age<18)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type Of Lesion (histo) | **Dorsal Aspect** | **Lateral Aspect** | **Tip Of Tongue** | **Ventral Aspect** |
| Benign Lesions | 4 (44.4%) | 1 (100%) | 0 no | 0 no |
| Lichenoid and undetermined significance Lesions | 1 (11.1%) | 0 no | 0 no | 0 no |
| Malignant Lesions | 1 (11.1%) | 0 no | 0 no | 0 no |
| Reactive, infectious and tumor like Lesions | 3 (33.3%) | 0 no | 10 (100%) | 12 (100%) |
| TOTAL | 9 (100%) | 1 (100%) | 10 (100%) | 12 (100%) |

**Table 4.** Distribution of tongue lesions according to categories and subsites in elderly patients (age >60)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type Of Lesion (histo) | **Dorsal Aspect** | **Lateral Aspect** | **Tip Of Tongue** | **Ventral Aspect** |
| Benign Lesions | 4 (12.5%) | 1 (1%) | 1 (5.6%) | 0 no |
| Immuno/autoimmune Lesions | 0 no | 8 (8.2%) | 0 no | 1 (8.3%) |
| Lichenoid and undetermined significance Lesions | 6 (18.8%) | 18 (18.4%) | 1 (5.6%) | 5 (41.7%) |
| Maligant Lesions | 2 (6.2%) | 28 (28.6%) | 0 no | 1 (8.3%) |
| Premaligant Lesions | 0 no | 15 (15.3%) | 0 no | 0 no |
| Reactive, infectious and tumor like Lesions | 20 (62.5%) | 28 (28.6%) | 16 (88.9%) | 5 (41.7%) |
| TOTAL | 32 (100%) | 98 (100%) | 18 (100%) | 12 (100%) |

**Table 5.** Distribution of tongue lesions according to categories and subsites (All ages)

p-value = 0.00049

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type Of Lesion (histo) | **Dorsal Aspect** | **Lateral Aspect** | **Tip Of Tongue** | **Ventral Aspect** |
| Benign Lesions | 13 (12.9%) | 6 (3.6%) | 1 (1.4%) | 0 no |
| Immuno/autoimmune Lesions | 0 no | 8 (4.8%) | 0 no | 2 (6.1%) |
| Lichenoid and undetermined significance Lesions | 12 (11.9%) | 27 (16.3%) | 1 (1.4%) | 6 (18.2%) |
| Maligant Lesions | 3 (3%) | 35 (21.1%) | 1 (1.4%) | 1 (3%) |
| Premaligant Lesions | 0 no | 17 (10.2%) | 0 no | 0 no |
| Reactive, infectious and tumor like Lesions | 73 (72.3%) | 73 (44%) | 70 (95.9%) | 24 (72.7%) |
| TOTAL | 101 (100%) | 166 (100%) | 73 (100%) | 33 (100%) |

**Table 6.** clinicopathological correlation according to subsites (All ages)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Match** | **Dorsal Aspect** | **Lateral Aspect** | **Tip Of Tongue** | **Ventral Aspect** |
| **Yes** | **68 (73.1%)** | **96 (62.3%)** | **63 (92.6%)** | **23 (76.7%)** |
| **No** | **25 (26.9%)** | **58 (37.7%)** | **5 (7.4%)** | **7 (23.3%)** |
| **TOTAL** | **93 (100%)** | **154 (100%)** | **68 (100%)** | **30 (100%)** |

**Figure. 1.** The incidence of tongue lesions according to type of lesion category

**Figure. 2.** Distribution of tongue lesions according to subsites

**Figure. 3.** Distribution of tongue lesions according to categories and subsites

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