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CLINICOPATHOLOGICAL ASSESSMENT OF LARYNGEAL LESIONS IN A SAMPLE OF IRAQI PATIENTS

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ABSTRACT

Background: Laryngeal lesions can create lot of mental and emotional tension in the patient and the family. Early diagnosis of the lesions can lead to effective management and good recovery. Histologically it is divided to benign, borderline and malignant, most common benign lesion is vocal cord nodule and most common malignant laryngeal lesion is squamous cell carcinoma. **Objective:** This study aims to assess the types of laryngeal lesions in a sample of Iraqi patient in correlation with clinicopathological parameters (age, sex, smoking history, lesion site , clinical presentation, grade of malignant lesions, pathological stage and lymph node status). **Methods:** A retrospective study of 83 randomly selected patients have laryngeal lesions collected from Teaching Laboratories of Ghazi Al-Harriri teaching hospital, from March 2018 to January 2023. **Results:** Laryngeal lesions found to be more frequent in male (78. 3%), the age group (51-60) years more than other age groups, benign lesions count (44.6%), borderline lesions (8.2%), malignant lesions (47.0%), hoarseness of voice was the common clinical presentation in all types of laryngeal lesions. Most patient with benign and borderline lesions were nonsmokers (63.9%) and (50%) respectively, while most patients with malignancy were smokers (65%). vocal cord nodule is the most common benign lesions (62.6%), moderate dysplasia is the most common dysplastic changes (57.1%) and squamous cell carcinoma is the most common laryngeal cancer(97.4%). **Conclusion:** Vocal cord nodule is the most common benign laryngeal lesions; squamous cell carcinoma isthe most common malignant laryngeal lesions. Age and smoking is the main risk factors for malignant transformation of laryngeal lesions.

INTRODUCTION

Laryngeal lesions can create lot of mental and emotional tension in the patient and the family. Early diagnosis of the lesions can lead to effective management and good recovery.[1]

Benign lesions of the larynx are classified into the commonly occurring non-neoplastic lesions and relatively rare neoplastic lesions.[2] The commonly encountered benign lesions of the larynx are: vocal cord polyps, vocal nodules, tuberculosis of larynx, laryngocele, laryngeal web, epiglottis cysts and subglottic haemangioma. Neoplastic lesions include papilloma, adenoma, chondroma and other non-neoplastic lesions like intubation granuloma, contact ulcer granulomaare relatively uncommon[3] The common sites of occurrence of the benign lesions of larynx are vocal cords, anterior commissure, false cords, epiglottis, aryepiglottic folds and ventricle in chronological order.[2] no neoplastic lesions of the larynx comprise 80% of the benign lesions diagnosed[4] the largest number of benign lesions in the age group of 21–50 years with a male: female (M: F) ratio of 2.6:1.[5] True benign tumors constitute 5% or less of all the laryngeal tumors. Out of them papilloma is the most common benign tumor, which accounts for 85% of cases.[3] The common factors responsible for the development of benign lesions are vocal abuse, exposure to various irritants like smoke, dust, fumes, alcohol etc.[2] Allergy and infective conditions of larynx (as Human papilloma virus in respiratory papillomatosis) are also responsible alone or in combination with other factors for the development of such lesions.[3]

Dysplasia is defined by a morphologic spectrum of architectural and cytological changes in the squamous mucosal epithelium that is associated with an increased likelihood of progression to SCC.[6] Tobacco and alcohol consumption are the most important single factors, other etiological factors involved in the genesis and progression of laryngeal dysplasia (LD) and squamous

cell carcinoma (SCC) include environmental factors (carcinogen exposure), genetic changes, epigenetic aberrations and immune escape.[7]

The vocal cords are affected most frequently by dysplasia, with rare involvement of thecommissure.[6]

At laryngoscopy, leukoplakia, erythroleukoplakia, hyperkeratotic lesions, mucosal reddening or thickening with exophytic tumor-like alterations may all be found in laryngeal dysplasia and no single clinical diagnosis should be considered pathognomonic for dysplasia.[7]

Over the years, many different grading schemes for dysplasia have been proposed, generally lesions that are traditionally considered as mild dysplasia would be categorized as "low grade" whereas lesions classified as moderate to severe dysplasia/ carcinoma in situ can be categorizedas "high grade."[6] based of the severity of the cytoarchitectural changes and risk of progression to invasive carcinoma.[8]

The rate of malignant transformation of dysplasia has been shown to be 14 per cent, with a mean time to transformation of 5.8 years and this risk rises with increasing severity of dysplasia.[9]

Laryngeal cancer is generally subdivided into supraglottic, glottic and subglottic cancer with squamous cell carcinoma (SCC) as the far most common histology type.[8] A minority of cases represent squamous cell variants, including verrucous carcinoma, sarcomatoid carcinoma, and neuroendocrine carcinoma.[10] Smoke and alcohol habits are the main risk factors, promoting a series of genetic mutations leading to invasive carcinoma.[8] Men are affected much more frequently than women, usually in the middle to later decades of life, although any age can be affected. Symptoms are nonspecific, with hoarseness, dyspnea, stridor, and dysphagia most common.[6] The mean age of patients is 65 years, with a higher proportion of males versus females, and blacks versus whites.[10]

Approximately 98% of laryngeal cancers arise in either the supraglottic or glottic regions, with glottic cancers being three times more common that supraglottic cancers, and subglottic cancers representing approximately 2% of all cases.[10]

Patients with laryngeal cancer are primarily treated with radiotherapy (accelerated or hyperfractionated) combined with the radiosensitizer Nimorazole. Small tumors, i.e., early stagetumors on the vocal cords may be treated surgically. Patients with locally advanced disease are treated with concomitant chemo-radiotherapy.[11]

The chances of survival for patients with laryngeal cancer is strongly related to the initial stage of disease, with cure rates of up to 80% to 90% for early stage T1 and T2 tumors. Conversely, the changes for survival decrease to as low as 40% in patients with stage IV disease at presentation.[12]

This study aims to assess the types of laryngeal lesions in a sample of Iraqi patient in correlation with clinicopathological parameters (age, sex, smoking history, lesion site, clinical presentation, grade of malignant lesions, pathological stage and lymph node status).

MATERIAL AND METHODS

A retrospective study including analysis of 83 randomly selected patients with laryngeal lesions collected from Teaching Laboratories of Ghazi Al-Harriri teaching hospital, from march 2018 to January 2023.

The clinic-pathological data that were collected from patient's pathology reports and hospital admission form included

- Age
- sex
- Clinical presentation
- History of smoking
- Type of surgical intervention (biopsy or total laryngectomy)
- lesion site
- histopathological diagnosis
- Grading and pathological staging for malignant lesions

Exclusion Criteria

Incomplete clinical or pathological data or laryngoscopy reports from referring physicians. (occupation, duration, laryngoscopic finding, reccurent lesions).

Formalin-fixed paraffin-embedded tissue blocks were collected. Then, sections 4-6 microns stained routinely with Hematoxylin & Eosin and the diagnosis was revised by two pathologists. All statistical analyses were performed utilizing SPSS, version 23 and including mean, frequency and percentage using Yates Chi square with p. value <0.05 regarded as statistically significant.

RESULTS

Age and sex distribution of studied samples

The total number of studied samples were 83 case. Regarding age, most of the them were in the age group 61-70 years (26.4%). The male to female ratio was 3.6:1 as illustrated in table (1)

Table (1): Age and sex distribution of all laryngeal lesions.

		Frequency	Percentage%
Age	1 - 10	3	3.6%
	11 - 20	1	1.2%
	21 - 30	5	6.0%
	31 - 40	15	18.0%
	41 - 50	15	18.0%
	51 - 60	19	22.8%
	61 - 70	22	26.4%
	>70	3	3.6%
	TOTAL	83	100%
Sex	Male	65	78.3%
	Female	18	21.7%
	TOTAL	83	100%

Histopathological characteristic of studied samples

37 case were benign lesions, 7 cases showed dysplastic changes and 39 cases were malignantlesions as shown in figure (1).

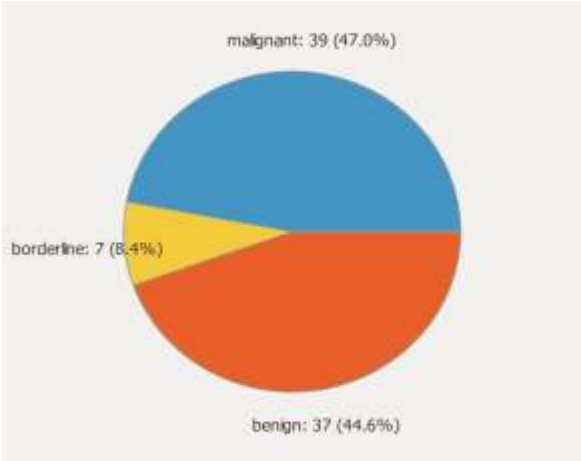

Figure (1): Histopathological distribution of all laryngeal lesions.

Age and sex distibution of benign laryngeal lesions

Regarding age, most of benign lesions were in the age group 31-40 year (27.0%), mean age is (40.67±16.08 SD). As for gender, the male to female ratio was (2.7:1) as illustrated in table (2)

Table (2): age and sex distribution of benign lesions.

		Frequency	Percentage%
Age	1 - 10	3	8.1%
	11 - 20	1	2.7%
	21 - 30	4	10.8%
	31 - 40	10	27.0%
	41 - 50	9	24.3%
	51 - 60	7	18.9%
	61 - 70	3	8.1%
	TOTAL	37	100%
Sex	Male	27	73.0%
	Female	10	27.0%
	TOTAL	37	100%

Clinical characteristic of benign lesions

The clinical characteristics of the benign studied sample are illustrated in table (3). hoarseness of voice was the most common presenting symptom (91.9%), and for cases of known history ofsmoking (36 case), 9/36 (25%) with negative history of smoking. the most common site was right vocal cord region 15/37(40.5%). As for histopathological diagnosis, benign laryngeal nodule was found in 23/37(62.2%) as illustrated in table (4).

Table (3): Clinical characteristic of benign lesions.

		Frequency	percentage %
Clinical presentation	hoarseness	34	91.9%
	dysphagia	1	2.7%
	shortness of breath	1	2.7%
	stridor	1	2.7%
	TOTAL	37	100.0%
Smoking	Smoker	9	25.00%
	ex-Smoker	4	11.10%
	not smoker	23	63.90%
	TOTAL	36	100%
Surgical Intervention Type	Biopsy	36	97.3%
	Laryngeal cystectomy	1	2.7%
	TOTAL	37	100.0%
Lesion Site	right vocal cord	15	40.5%
	left vocal cord	10	27.0%
	bilateral vocal cord	5	13.5%
	supraglottic	5	13.5%
	Anterior commissure	1	2.7%
	TOTAL	37	100%

Table (4): Frequency of histopathological diagnosis of benign lesions.

		Frequency	Percentage%
Histopathologicaldiagnosis	Benign laryngealnodule	23	62.2%
	benign laryngeal polyp	3	8.1%
	Benign larengealnodule	2	5.4%
	Benign laryngeal cyst	2	5.4%
	Laryngeal papillomatosis	2	5.4%
	papilloma	2	5.4%
	Acute suppurativelaryngitis	1	2.7%
	laryngocele	1	2.7%
	Pemphigus vulgaris	1	2.7%
	TOTAL	37	100.0%

Age and sex distribution of borderline laryngeal lesions

Regarding age, the age distribution ranging from (21-60) year most lesions were in the age group 41-50 year (42.9%), mean age is (45.42±12.06 SD). As for gender, the male to femaleratio was (2.5:1). as illustrated in table (5).

Table (5): Age and sex distribution of borderline lesions.

		Frequency	Percentage%
Age	21 - 30	1	14.3%
	31 - 40	1	14.3%
	41 - 50	3	42.9%
	51 - 60	2	28.6%
	TOTAL	7	100%
Sex	Male	5	71.4%
	Female	2	28.6%
	TOTAL	7	100%

3.6 Clinical characteristic of borderline lesions

The clinical characteristics of the borderline studied sample are illustrated in table (6). hoarseness of voice was the most common presenting symptom (85.7%), 6 cases with known history of smoking, 3/6(50%) with negative history of smoking. the most common site was left vocal cord region (57.1%). As for histological type 57.1% showed moderate dysplasia, figure (2).

Table (6): clinical characteristic of borderline lesions.

		Frequency	percentage %
Clinical history	hoarseness	6	85.7%
	shortness of breath	1	14.3%
	TOTAL	7	100.0%
Smoking	Smoker	1	16.7%
	ex-Smoker	2	33.3%
	not smoker	3	50.0%
	TOTAL	6	100.0%
Surgical Intervention Type	Biopsy	7	100.0%
	TOTAL	7	100.0%
Lesion Site	left vocal cord	4	57.1%
	right vocal cord	2	28.6%
	bilateral vocal cord	1	14.3%
	TOTAL	7	100.0%

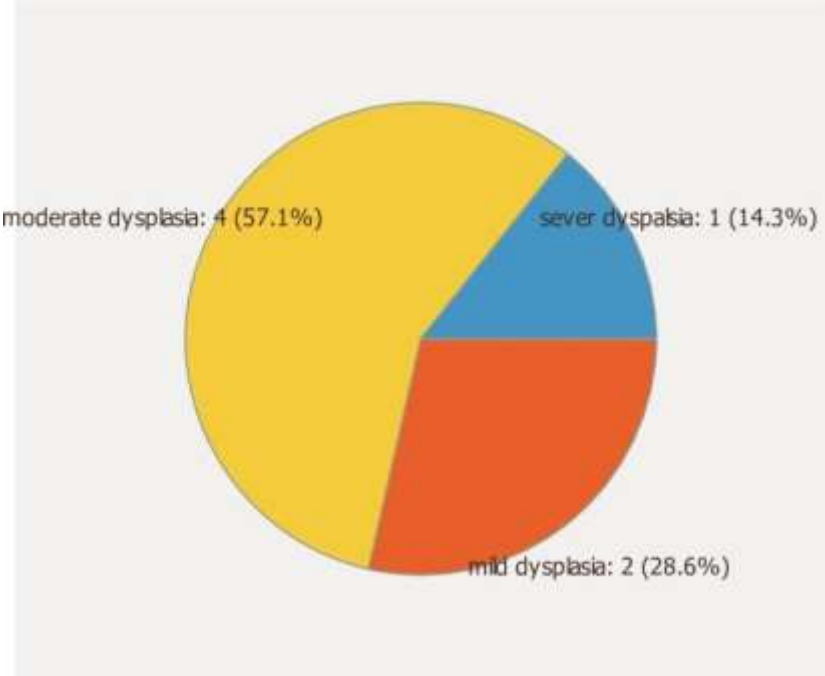

Figure (2): Frequency of histopathological diagnosis of borderline lesions.

Age and sex distribution of malignant lesions

Regarding age, most of the malignant cases were in the age group 61-70 year (48.6%) mean age is (59.6±10.5 SD). As for gender, male to female ratio (5.5:1), as illustrated in table(7).

Table (7): Age and sex distribution of malignant lesions.

		Frequency	Percentage %
Age	31 - 40	4	10.4%
	41 - 50	3	7.7%
	51 - 60	10	25.8%
	61 - 70	19	48.6%
	> 70	3	7.8%
	TOTAL	39	100%
Sex	Male	33	84.6%
	Female	6	15.4%
	TOTAL	39	100%

Clinical characteristic of malignant lesions

The clinic-pathological characteristics of the studied sample are illustrated in table (8). hoarseness of voice was the most common presenting symptom (82.1%), regarding smoking status, 37 cases with known history of smoking (2 cases were excluded with unknown smoking history) 24/37 (64.9%) are smokers. by laryngoscope biopsies and total laryngectomy evaluation of lesion site 31 case with known lesion site (8 cases out of 39 were excluded), the most common site was supraglottic region 11/31 (35.5%). for histopathological characteristic of malignant lesions as illustrated in table (9), squamous cell carcinoma was found in 38/39 (97.4%), mostly keratinized SCC (84.2%) whereas only 1 /39 (2.6%) was adenoid cystic carcinoma, in Concerning tumor grading, most lesions were moderately differentiated 17/39 (43.6%), as for tumor staging(17 cases have been excluded with unknown tumor stage), most cases with known stage were T3 and T4a 9/22 (40.9%) for each stage, regarding lymph nodes most cases 16/22 (72.7%) were seen with N0.

Table (8): Clinical characteristic of malignant lesions.

		Frequency	percentage%
Clinical presentation	hoarseness	32	82.1%
	neck swelling	2	5.1%
	shortness of breath	2	5.1%
	stridor	2	5.1%
	dysphagia	1	2.6%
	TOTAL	39	100%
Smoking history	Smoker	24	65%
	ex-Smoker	9	24%
	not smoker	4	11%
	TOTAL	37	100%
Surgical Intervention Type	total laryngectomy	23	59.0%
	Biopsy	16	41.0%
	TOTAL	39	100%
Lesion Site	supraglottic	11	35.5%
	supraglottic and glottic	9	29.0%
	glottic	4	12.9%
	left vocal cord	4	12.9%
	glottic and subglottic	2	6.5%
	subglottic	1	3.2%
	TOTAL	31	100%

Table (9): Frequency of histopathological diagnosis of malignant lesions.

		Frequency	Percentage %
Histopathologicaldiagnosis	SCC	38	97.4%
	adenoid cystic ca	1	2.6%
	TOTAL	39	100%
SCC subtypes	keratinized	32	84.2%
	verrocus	3	7.9%
	sarcomatoid	2	5.3%
	papillary	1	2.6%
	TOTAL	39	100%
Grade	moderate	17	43.6%
	poorly	10	25.6%
	well	10	25.6%
	high grade	1	2.6%
	undifferentiated	1	2.6%
	TOTAL	39	100%
Pathological Stage	T3	9	40.9%
	T4a	9	40.9%
	T2	4	18.2%
	TOTAL	22	100%
Lymph nodeinvolvement	N0	16	72.7%
	N1	1	4.5%
	N2	1	4.5%
	N3	1	4.5%
	NX	3	13.6%
	TOTAL	22	100%

Correlation between histopathological diagnosis and clinical parameters

Significant association was detected between histopathological diagnosis and age (p value=0.035), and highly significant association with smoking (p value=0.001), while regarding sex and clinical presentation, there were no significant association (p value = 0.421), (p value= 0.964) respectively as illustrated in table(10).

Table (10): Correlation between histopathological diagnosis according to age groups, sex, clinical presentation and smoking history.

Correlation between histopathologicaldiagnosis and clinical parameters	P-value
Histopathological diagnosis and age	0.035
Histopathological diagnosis and sex	0.421
Histopathological diagnosis and clinicalpresentation	0.947
Histopathological diagnosis andsmoking	<0.001

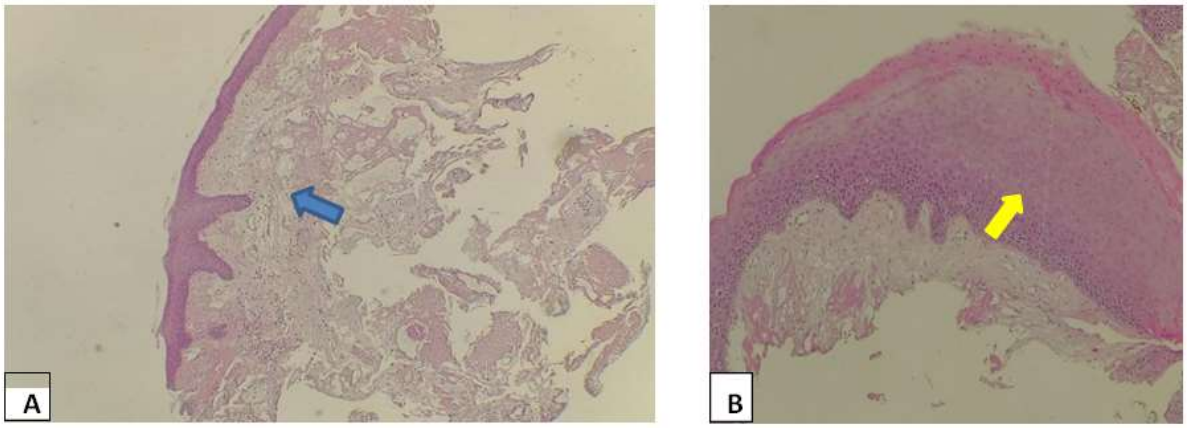

Figure 3: Vocal cord nodule; section shows myxo-hyallin stroma (blue arrow) lined by squamous epithelium with unremarkable changes (yellow arrow). H&E (A) 4X, (B) 10X.

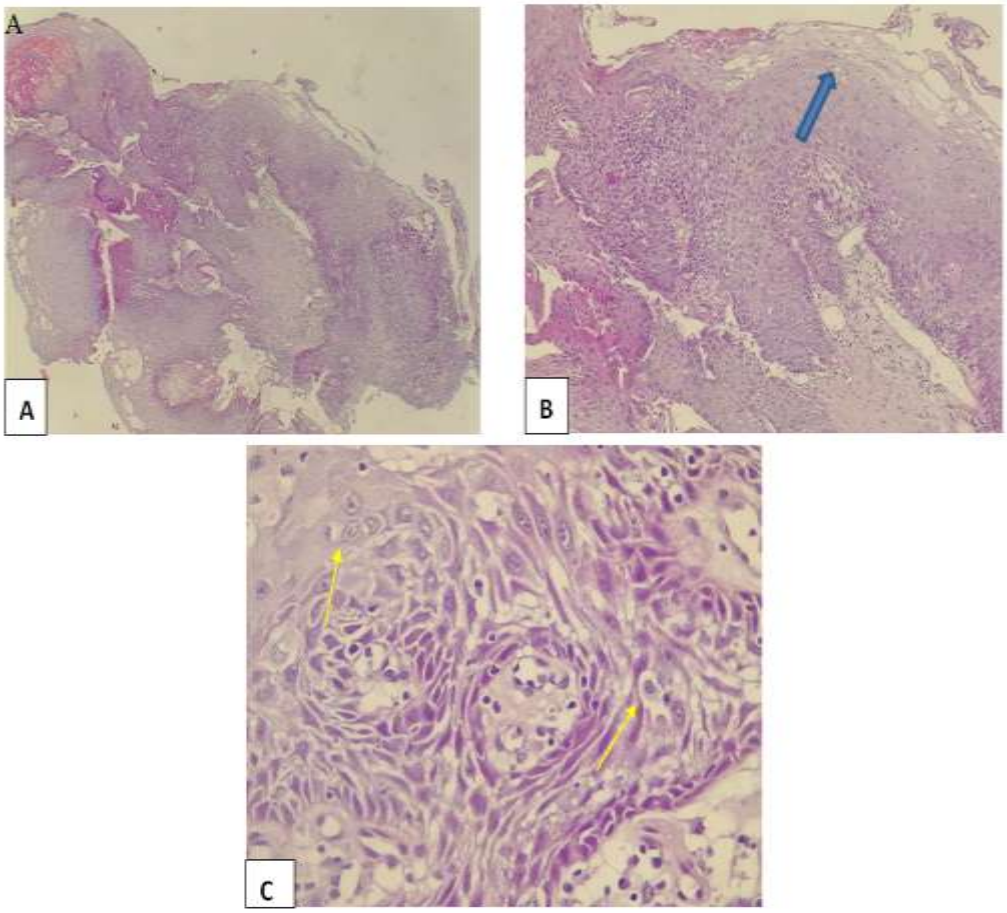

Figure 4: Moderate dysplasia of larynx; section shows moderate nuclear atypia with prominent nulei(yellow arrow) with retained mturation and stratification of upper layers (bluearrow).H&E (A)4x, (B)10x,C(40x).

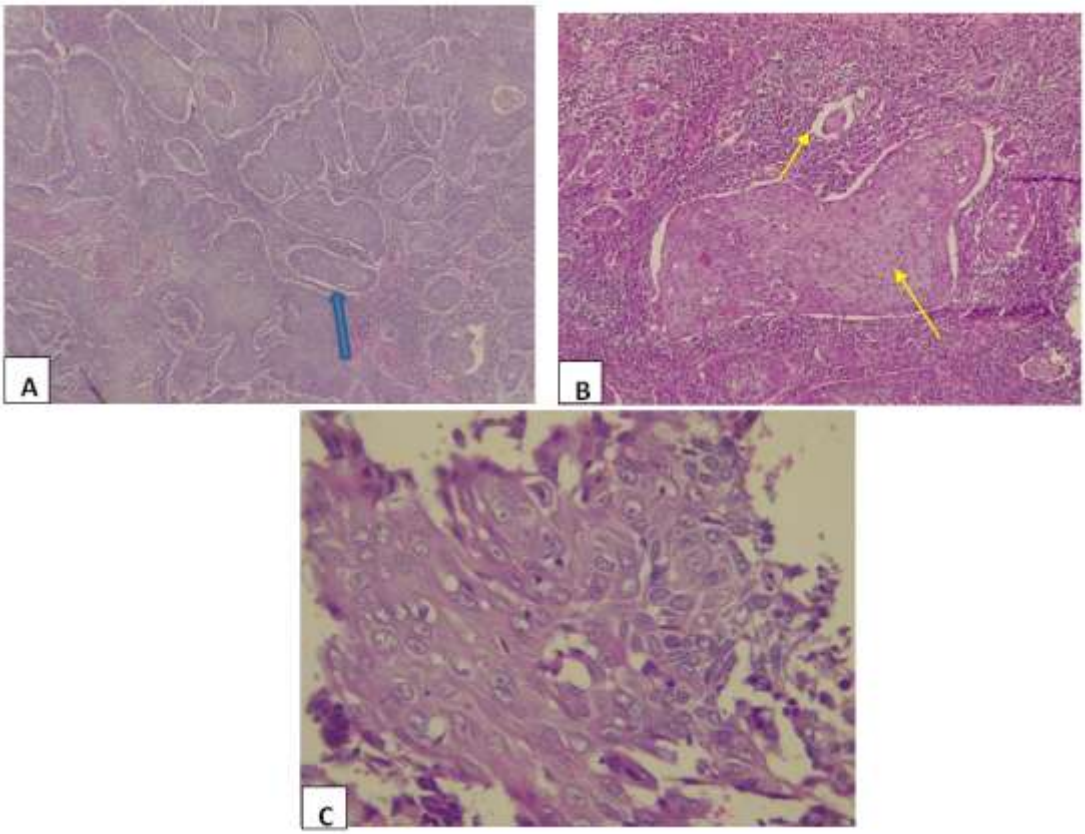

Figure 5: Moderately differentiated squamous cell carcinoma; section shows nesting and sheets of pleomorphic cells (blue arrow) with areas of keratin pearls invade inflamed submucosa (yellow arrow). H&E (A) 4x (B) 10x, (C) 40x.

DISCUSSION

Majority of the results of this study were in concordance with the results of other similar studies. In the current retrospective case series study which was done on 83 cases of laryngeallesions.

Sociodemographic distribution

In this study, the mean age of all laryngeal lesions is 50, this result in agreement with the findings of Anis M.[13] Most benign lesions are in the (31-40) age group, borderline lesions mainly in (41-50) age group and malignant lesions in (61-70) age group, there is a statistical relationship between age group and lesion type with **p-value = 0.035,** these results are in agreement with other study in Iraq and India which are conducted by Hegde M. et al, Atiyah H. and others.[1,21, 25,28]

Regarding the sex, in total studied sample, male (78.3%) is higher prevalence than female (21.7%). the male: female ratio was 2.7:1 in benign lesions, 2.5:1 in borderline lesion and 5.5:1in malignant lesions, there was no statistical relationship between sex and lesion type, P **value** =0.421 similar finding was reported by Malik P. et al in India & others (14,17, 28) but Chan T. et al found two third of benign lesions are female (19).

Clinicopathological characteristics

In this current study, the most common clinical presentation is hoarseness of voice, (91.9%) in benign lesions, (85.7%) in borderline lesions and (82.1%) in malignant lesions, these results are in agreement with other studies which are conducted by Hegde M. et al, Qahtan M. et al.[1,16,29]

Regarding smoking history, (63.9 %) of benign lesions patients were nonsmoker, (50%) of borderline lesion patients were not smoker while (65%) of patient with malignant lesion were smoker, (24%) were ex-smoker. there was highly significant relationship between smoking and lesion type P value=0.001. these results also have been found in other studies.[19,17,27] but Chu F.et al ,who showed that most patients with borderlines lesions are either smoker or ex-smoker (36.3%) and (43.18%) respectively.[8] These differences could be due to sample collection bias.

In this study, The most common site of benign lesions was vocal cords with (40.5%) on the right vocal cord, (27.0%) on the left vocal cords, this result is in agreement with Wani A. et al study,[21] while Singhal P. et al found most benign lesions are observed in left vocal cord.[5] These differences could be due to the difference in sample sizes.

Regarding site of malignant lesions, mostly found in supraglottis (35.5%), this result is in agreement with study which was conducted by Ahmed S. et al.[26] but different from Qahtan M. et al and Kitcher E. et al studies

which reported that glottis is the most common site of malignant lesions.[16,24]

Histopathological characteristics

In this study, (44.6%) were benign lesions (8.4%) were borderline lesions and (47%) were malignant, this result is going with Anis M. et al study in USA, which found 50% of all the laryngeal lesions biopsied were benign, whereas the rest were either dysplastic or malignant lesions.[13]

The vocal cord nodule (62.2%) is the predominant benign lesions of larynx, followed by vocal cord polyp (8.1%) this result agrees with study USA (18). But the vocal cords polyp was most frequent on other studies in India and Netherland (5,14,23) this regard to differences in culture and place of researches.[18]

The initial microscopic change in laryngeal dysplasia is believed to be in the basal layer of the epithelium. The premalignant changes progress gradually toward the surface, spreading also laterally in all directions within the epithelial layer.[29] the most common system used for laryngeal premalignancy pathological diagnosis is WHO 2005 classification system.[29]

According to WHO classification laryngeal lesions are classified in to mild dysplasia, moderate dysplasia, severe dysplasia and CIS.[20] In the current study, moderate dysplasia was the most common dysplastic changes in the larynx (57.1%) this result is agreement with study which is conducted by Dispenza F. et al,[30] but it is different from another study which showedsever dysplasia is the most common dysplasia(27.82%),[29] and another study showed mild dysplasia is the most common type of dysplasia,[8] This variation could be due to that there is a subjective element in the grading of laryngeal dysplasia by pathologists, which results in controversy and limitation in diagnosing laryngeal dysplasia even though the same classification system is employed,[29] Different dysplastic grades could be given by different pathologists in their independent evaluation to the same case, and also there may be a possibility that even the same pathologist could give different results for the same intricate case at a different time.[29]

In current study, the most common type of malignant lesions is SCC (97.4%), and most of them were moderately differentiated (43.6%). this result is very closely to study which conducted by Qahtan M. et al, which found SCC is (100%) of laryngeal cancer and most of them are well andmoderate differentiated.[16]

Regarding the staging, most samples were equally found in T3 and T4a (40.9%) and T2 in (18.2%), this results agreed with that of Lydiatt W. et al, who stated that the most common stage of laryngeal cancer at presentation were stage III and IV especially for supraglottic this was because this area was rich in lymphatic and associated with high percentage of lymph nodemetastasis.[15]

Regarding L.N metastasis, (72.7%) with N0, this result is in agreement with Ahmed S.et al study, who found (76.5%) of laryngeal cancer is N0 metastasis.[26]

CONCLUSION

Vocal cord nodule is the most common benign laryngeal lesions; squamous cell carcinoma is the most common malignant laryngeal lesions. Age and smoking is the main risk factors for malignant transformation of laryngeal lesions.

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