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Original research article

Cytological study of salivary gland lesions at Jhalawar Medical College

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Abstract

Background: Fine needle aspiration cytology (FNAC) is safe reliable, cost effective & minimally invasive method for evaluating salivary gland lesions owing to its easy accessibility & superficial location. The objective of this study was cytological study of salivary gland lesion.

Methods: This prospective study was carried out in the Department of Pathology, Jhalawar Medical College and SRG Hospital, Jhalawar. The study was comprise of all patients of salivary gland lesions of either sex and age admitted/attending in our hospital after considering inclusion and exclusion criteria.

Results: The sensitivity of the cytopathological diagnosis was 64.29%, specificity was 95.45%, positive predictive value was 81.82%, and negative predictive value was 89.36, and accuracy was 87.93% considering histopathology as gold standard.

Conclusion: FNAC as a safe, simple, rapid, reliable, cost-effective, and well tolerated preoperative procedure with minimal morbidity carried out in outpatient department yielding accurate diagnosis of inflammatory, benign, and malignant salivary gland lesions with good sensitivity and specificity.

Keywords: FNAC, Cytopathological, sensitivity, Specificity

Introduction

Salivary glands are exocrine organs. There are three paired major salivary glands (parotid, submandibular, sublingual) and numerous unpaired minor salivary glands. It is made of lobular architecture of tubuloacinar glands which is well defined by anastomosing connective tissue trabeculae carrying excretory ducts, vascular & neural branches. Salivary glands are widely distributed throughout the mouth and oropharynx.[1] The causes of salivary gland lesions are different, like inflammatory process, cysts, or tumors, and often it is difficult to say whether the swelling is arising from salivary gland proper or from adjacent structures such as lymph nodes, soft tissues, or skin.[2]

Fine needle aspiration cytology (FNAC) is safe reliable, cost effective & minimally invasive method for evaluating salivary gland lesions owing to its easy accessibility & superficial location. It is a useful method for evaluating suspicious salivary glands lesions due to its minimum morbidity, rapid turnaround time, high specificity, and sensitivity.[3] FNAC is minimal risk procedure than conventional biopsy procedure. Schröder et al.[7] mentioned that FNAs have a minimal incidence of complication, have a reduced risk of tumor cell

implantation (<1%). In addition, complications from surgical procedures such as hemorrhage, facial nerve damage and inflammatory reaction at the surgical site are rare.[4]
Fine-needle aspiration cytology (FNAC) is the first tissue-based procedure applied before any surgical intervention. It has now been widely accepted by head and neck surgeons as an excellent though challenging, the primary method of evaluating the space occupying lesions of salivary gland.[5]

Materials and Methods
This prospective study was carried out in the Department of PATHOLOGY, Jhalawar Medical College and SRG Hospital, Jhalawar.The study was comprise of all patients of salivary gland lesions of either sex and age admitted/attending in our hospital after considering inclusion and exclusion criteria.

Source of data
The study will comprise of all patient with salivary gland lesion admitted/attending OPD in our hospital.

Inclusion criteria
- All palpable masses in major and minor salivary glands with or without pain in head and neck region.

Exclusion criteria:
- Non palpable masses
- Uncooperative subjects

Study period:
Over a period of 2 year from June 2018 to May 2020.

Sample size
The sample size of 153 was determined by power analysis; due to the preliminary study results. All statistical analyses results are performed by using SPSS 24.0 software package (SPSS Inc., Chicago, IL, USA). A $p < 0.05$ will be accepted as statistically significant.
Methodology-
a. After obtaining approval and clearance from the institutional ethical committee, only those patients meeting the inclusion and exclusion criteria will be enrolled for the study.
b. Informed consent will be obtained from each patient.
c. After enrollment the following parameters will be noted in all patients: Detailed clinical data, family history, personal history, physical examination and relevant investigations.

Results
A prospective study was conducted in the department of pathology, Jhalawar medical college & hospital from June 2018 to may 2020. A total of 185 cases were included in the study. Histopathological follow up was possible in 58 cases. We have found that maximum number 77(42%) of the cases belong to the age group of 21 to 40 years of age i.e., third and fourth decade followed by 25% in 41-60 years of age and so on. It is quite less in no. above the age group of 70 years. 52% cases are males and rest 47% cases are females.

Table 1: Distribution of the salivary gland lesions according to Site

Site	Number	Percentage (%)
Parotid	86	46.49
Right	49	26.49
Left	37	20
Submandibular	79	42.7
Right	42	22.7
Left	34	18.38
Bilateral	3	1.62
(MSG)	20	10.81
Floor of mouth	10	5.41
Hard palate	4	2.16
Upper lip	2	1.08
Buccal mucosa	2	1.08
Lower Lip	1	0.54
Tongue (MSG)	1	0.54
Grand Total	185	100

The above table depicts the distribution of cases as per the site wise, which is in detailed side as compared to the previous tables in terms of three major categories. In both parotid gland and submandibular gland, right side (49%) is more common than left side (38%). Among MSG, floor of mouth is the most common location (5%) followed by the hard palate (2%).

Table 2: Distribution of the cytopathological cases according to MSRSGC

N=185	Number (n)	Percentage %
I (Non -Diagnostic)	9	4.86
II (Non -Neoplastic)	95	51.35
C.SIALADENITIS	47	25.41
MUCOCELE	20	10.81
A. SIALADENITIS	10	5.41
G. SIALADENITIS	8	4.32
SIALADENOSIS	5	2.7
REACTIVE LNH	3	1.62
LYMPHOEPITHELIAL CYST	1	0.54
SALIVARY DUCT CYST	1	0.54
III (AUS)	5	2.7
AUS	5	2.7
IV A (Neoplasm: Benign)	59	31.89
PA	50	27.03
WARTHIN TUMOUR	6	3.24
LIPOMA	1	0.54
ONCOCYTOMA	1	0.54
SPINDLE CELL NEOPLASM	1	0.54
IV B (SUMP)	3	1.62
BASALOID NEOPLASM	3	1.62
V (Suspicious for Malignancy)	2	1.08

VI (Malignant)	12	6.49
MEC	6	3.24
AdCC	3	1.62
CA Ex PA	2	1.08
AcCC	1	0.54

The above table depicts the distribution of salivary gland lesions as per cytological diagnosis according to MSRSGC. Among non-neoplastic (II) category, most common is chronic sialadenitis (25.41%). Among the benign neoplasm (IV A), most common is pleomorphic adenoma (27.03%). And mucoepidermoid carcinoma is the most common malignant salivary gland tumor (3.24%).

Table 3: Distribution of the cases according to adequacy rate

Adequacy	Number	Percentage (%)
Adequate	176	95.14
Non adequate	9	4.86
Grand Total	185	100.00

The above table depicts the distribution of cases as per adequacy where we have found that 95.14% of the cases are adequate and less than 4.86% are non adequate

Table 4: Distribution of the cases according to benign and malignant lesions

Type	Number	Percentage (%)
Benign	168	90.81
Malignant	17	9.19
Total	185	100.00

The above table depicts the distribution of the cases as per Cytopathological Diagnosis where we have found that 90% of cases belong to benign and rest belong to malignant

Table 5: Distribution of the cytopathological cases according to site and MSRSGC

	Total	Parotid gland	Sub mandibular gland	Floor of mouth (msg)	Hard palate (msg)	Buccal mucosa (msg)	Lip (msg)	Tongue (msg)	P-values LS
I	9	5(55.56)	4(44.44)	0	0	0	0	0	<0.001S
II	95	25 (26.32)	58(61.05)	8(8.42)	0	2 (2.11)	1(1.05)	1 (1.05)	
C. Sialadenitis	47	8(17.02)	39(82.98)	0	0	0	0	0	<0.001S
Mucocele	20	1(5)	7(35.00)	8(40.00)	0	2(10)	1(5)	1(5)	<0.001S
A. Sialadenitis	10	5(50.00)	5(50.00)	0	0	0	0	0	<0.001S
G. Sialadenitis	8	5(62.5)	3(37.5)	0	0	0	0	0	<0.001S
Reactive lnh	3	3(100)	0	0	0	0	0	0	<0.001S
Sialadenosis	5	2(40)	3(60)	0	0	0	0	0	0.008S
Lymphoepithelial cyst	1	1(100)	0	0	0	0	0	0	0.342NS
Salivary duct cyst	1	0	1(100)	0	0	0	0	0	0.342NS
III	5	4(80)	1(20)	0	0	0	0	0	<0.001S
IVA	59	43(72.88)	3(5.08)	0	2(3.39)	0	1(1.69)	0	
PA	50	34(68.00)	13(26.00)	0	2(4.00)	0	0	0	<0.001S
Warthin tumor	6	6(100)	0	0	0	0	0	0	<0.001S
Spindle cell neoplasm	1	1(100)	0	0	0	0	0	0	0.342NS

Lipoma	1	1(100)	0	0	0	0	0	0	0.342NS
Oncocytoma	1	1(100)	0	0	0	0	0	0	0.342NS
IV B	3	0	0	1(33.33)	1(33.33)	0	1(33.33)	0	0.564NS
V	2	1(50)	1(50)	0	0	0	0	0	0.446NS
VI	12	8(66.67)	2(16.67)	1(8.33)	1(8.33)	0	0	0	<0.001S
MEC	6	5(83.33)	1(16.67)	0	0	0	0	0	<0.001S
AdCC	3	1(33.33)	1(33.33)	1(33.33)	0	0	0	0	0.564NS
Ca Ex PA	2	2(100)	0	0	0	0	0	0	0.021S
AcCC	1	0	0	0	1(100)	0	0	0	N/A
Grand Total	185	86	79	10	4	2	2	1	

In this table, there is distribution of all salivary gland lesions according to site and MSRSGC in which we have found that in ND category, all cases are distributed in parotid and submandibular gland without any lesions in MSG. In II category, maximum lesions are in submandibular gland (58%) in which there are a greater number of cases of chronic sialadenitis (83%). Most common site of mucocele is floor of the mouth (40%) followed by 35% in submandibular gland.

In III category, 80% cases are in parotid gland and 20% cases are in submandibular gland.

Among IVA category, 73% cases are distributed in parotid gland. Pleomorphic adenoma is most common in parotid gland (68%) and it is found in hard palate and upper lip among MSG. There are 6 cases of Warthin tumor and all cases (100%) are found in parotid gland only. In IVB category, there are 3 cases of basaloid neoplasm and all are in MSG; 1 in floor of mouth, 1 in hard palate and 1 case in upper lip.

In V category, there are 2 cases of PA with atypia with one each in parotid and submandibular gland. In VI (malignant) category, most common is mucoepidermoid carcinoma of which 83% cases are in parotid gland. Adenoid cystic carcinoma is found in parotid, submandibular, and floor of mouth with equal percentage (33.33%).2 cases of carcinoma ex pleomorphic adenoma is found in parotid gland.1 case of acinic cell carcinoma is found in hard palate.

Table 6: Distribution of the cases according to Histopathological Diagnosis

	Histopathological Diagnosis	Number	Percentage (%)
	done	58	31.35
	Histopathological Diagnosis		
Non-Neoplastic	C. SIALADENITIS	11	18.97
	MUCOCELE	5	8.62
Neoplastic Benign	PA	22	37.93
	WARTHIN TUMOUR	4	6.9
	CANALICULAR ADENOMA	2	3.45
Malignant	MEC	6	10.34
	AdCC	3	5.17
	Ca Ex Pa	2	3.45
	AcCC	2	3.45
	SALIVARY DUCT CA	1	1.72

The above table depicts the distribution of cases as per histopathological diagnosis. Among 185 cytopathology cases, 58 patients came for histopathology in our department i.e.,32% of cytopathological cases. We have found that maximum number of cases are of PA i.e., 37.93% followed by C. Sialadenitis 18.97% and so on. Among the malignant cases, MEC is the most common one (10.34%).

Table 7: Cyto-histopathological correlation

Milan category	Cytopathological Diagnosis	Histopathological diagnosis	
		Benign	Malignant
I (ND)	Cystic Lesion (4)	PA (1) WARTHIN TUMOUR (1)	AcCC (1) CA Ex PA (1)
	Scanty (1)	C. SIALADENITIS (1)	
	Blood Mixed (1)	PA (1)	
II (NN)	C. SIALADENITIS (8)	C. SIALADENITIS (7)	MEC (1)
	MUCOCELE (5)	MUCOCELE (5)	
III (AUS)		C. SIALADENITIS (3)	MEC (2)
IV A (B)	PA (20)	PA (20)	
	WARTHIN TUMOUR (3)	WARTHIN TUMOUR (3)	
IV B (SUMP)	Basaloid Neoplasm (3)	CANALICULAR ADENOMA (2)	AdCC (1)
V (SM)	PA with Atypia (1)		CA Ex PA (1)
VI (M)	MEC (3)		MEC (3)
	AdCC (2)		AdCC (2)
	AcCC (1)		AcCC (1)

This table showed that in I category, 4 Benign and 2 malignant cases were observed. There are 4 cystic lesions in non diagnostic category. On histopathology, it came out to be pleomorphic adenoma and Warthin tumor in benign lesions and acinic cell carcinoma and carcinoma ex pleomorphic adenoma in malignant lesions. In category II; only one case of chronic sialadenitis turn out to be malignant i.e., mucoepidermoid carcinoma and rest are benign. In category III; 2 cases are diagnosed as mucoepidermoid carcinoma in which there was abundant mucoid aspirate only without any epithelial cells on cytopathology. In category IV A: no discordant cases were observed. In category IV B; out of 3 basaloid neoplasm, 2 cases are of canalicular adenoma (benign) and 1 case of AdCC (malignant). In category V: 1 case of PA with atypia was diagnosed as CA Ex PA (1) on histopathology. In VI category (malignant), all cases are malignant on histopathology.

The sensitivity of the cytopathological diagnosis was 64.29%, specificity was 95.45%, positive predictive value was 81.82%, and negative predictive value was 89.36, and accuracy was 87.93% considering histopathology as gold standard.

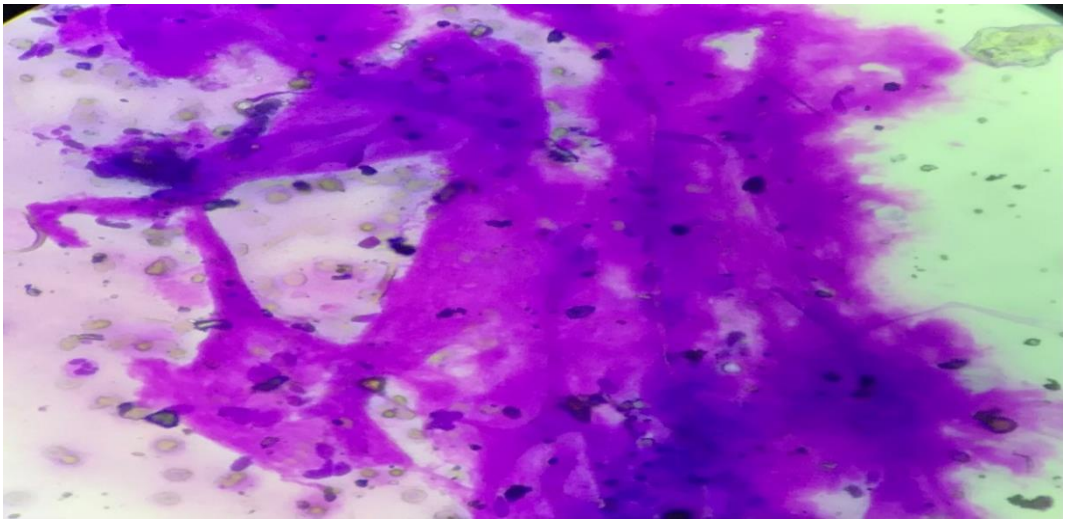

Figure 1: Pleomorphic Adenoma Showing Fibrillar Fibromyxoid Stroma (Field Stain) 40x

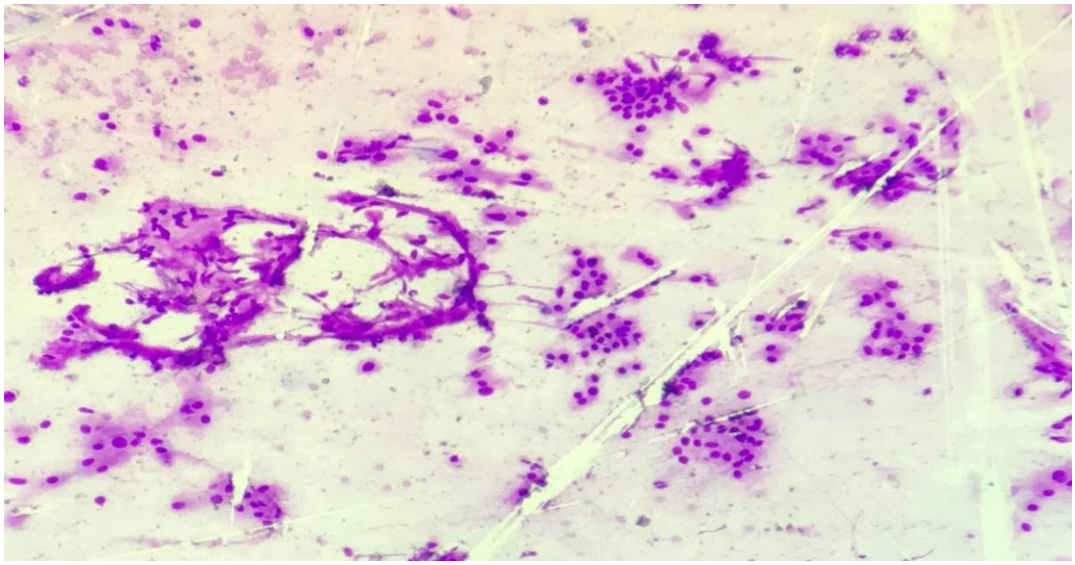

Figure 2: Pleomorphic Adenoma Showing Poorly Cohesive Epithelial Like Cells And Fibrillar Fibromyxoid Stroma Including Single Oval And Spindle Cells (Field Stain) 10x

Discussion

Our study depicts the distribution of cases as per MSRSGC where we have found that rate of I (ND) category was 4.86% (9/185). II (NN) category accounted for maximum no. of cases with 51.35% (95/185). Category III (AUS) had 2.7% (5/185) cases while IVA (NB) category had 31.89% (59/185) of cases. IVB (SUMP) category included 1.62% (3/185) and V (SM) had 1.08% (2) cases only. VI (M) category had 6.49% (12/185) of cases. Similar findings were observed in other studies as Kala C et al (2019)[6]observed the distribution of cases into different categories was as follows ND (6.1%), NN (38.2%), AUS (2.7%), NB (33.4%), SUMP (2.0%), SM (2.4%), and M (15%). Mukundapai M et al (2020)[7]categorized the cases as ND (1.58%), NN (13.43%), NB (30%), AUS (0.8%), and SM and M category (51.8%).

In our study, among NN (II)category, most common is chronic sialadenitis 49.47% (47/95). Among the NB (IV A), most common is pleomorphic adenoma 84.74% (50/59) followed by Warthin tumor (10%). And mucoepidermoid carcinoma is the most common malignant salivary gland tumor 50% (6/12). The predominance of these neoplasms was similar to those previously reported in as Pujani et al (2018)[8]observed that cases in ND(I) aspirations was 4.6% (7/150). NN(II) category accounted for 42% (63/150) with the most frequent diagnosis being sialadenitis 55.5% (35/63) followed by sialadenosis 19% (12/63). Category (III) AUS had 2% cases while category IVA (NB) comprised of maximum no. of cases 43.3%, out of which pleomorphic adenoma (PA) was the most common. Cases in SUMP(IVB) and SM(V) category was 1.33% each, while M (VI) category had 5.33% cases.

The main goal of FNA is to determine if a mass is inflammatory and/or reactive, benign or malignant neoplasm and if possible, to render a specific diagnosis, especially typing the neoplastic lesions. Cytology study is definitely distinguishing between salivary and nonsalivary lesions, benign and malignant lesions, so also specific and nonspecific inflammation. Because of heterogeneity of salivary gland lesions and overlapping cytomorphological features, it poses a problem in the definitive diagnosis.

Among 185 cytopathology cases, 58 patients came for histopathology in our department i.e.,32% of cytopathological cases. We have found that maximum number of cases are of PA i.e., 37.93% followed by C. Sialadenitis 18.97%. Among the malignant cases, MEC is the most common one (10.34%).

We have observed that 51 cases were concordant and rest 7 were discordant. This study showed that in I category, 4 Benign and 2 malignant cases were observed. There are 4 cystic

lesions in non diagnostic category. On histopathology, it came out to be pleomorphic adenoma and Warthin tumor in benign lesions and acinic cell carcinoma and carcinoma ex pleomorphic adenoma in malignant lesions. Cystic salivary gland lesions are an important diagnostic pitfall[9]. Cystic lesions can range from a non-neoplastic lesion like simple retention cyst to benign tumors like Warthin's tumor to malignant tumors like mucoepidermoid carcinomas. Most cystic lesions aspirations yield fluids which are poorly cellular making cytological diagnosis very tricky. Studies have suggested that diagnostic yield can be increased by reaspiration under radiological guidance.

In category II; only one case of chronic sialadenitis turn out to be malignant i.e., mucoepidermoid carcinoma and rest are benign. In category III; 2 cases are diagnosed as mucoepidermoid carcinoma in which there was abundant mucoid aspirate only without any epithelial cells on cytopathology. Our findings are similar to that of Cohen et al. (1986)[10] and Hajdu and Melamed (1984)[11].Mucoepidermoid carcinoma, although the most common malignant tumor of major salivary glands, poses a diagnostic challenge in cytopathology. The false negative interpretation is due to various reasons including paucicellularity, cystic fluid diluting tumor cells, presence of inflammatory cells, and degenerated epithelial cells in the aspirates. Misinterpretations are common as the bland-looking intermediate cells are mistaken as benign salivary gland cells and the scattered mucinous tumor cells are mistaken for histiocytes or mucus-containing macrophages.

In category IV A: no discordant cases were observed. Pleomorphic adenomas commonly exhibit a metachromatic fibrillary and frayed stroma which make their diagnosis simple.

In category IV B; out of 3 basaloid neoplasm, 2 cases are of canalicular adenoma (benign) and 1 case of AdCC (malignant). Adenoid cystic carcinoma on cytology shows variable cellularity with small monotonous looking basaloid tumor cells and acellular homogeneous nonfibrillary extracellular matrix which takes different shapes from branching tubules, cylinders, to spheres. A distinctive feature of adenoid cystic carcinoma is its sharp interface between the matrix and tumor cells. Hyaline globules are not very specific for adenoid cystic carcinoma and can occur in basal cell adenoma, polymorphous low-grade adenocarcinoma, basal cell adenocarcinoma, epithelial myoepithelial carcinoma, and even basaloid squamous cell carcinoma. [7]

In category V: 1 case of PA with atypia was diagnosed as CA Ex PA (1) on histopathology. In VI category (malignant), all cases are malignant on histopathology.

Kakoty S et al (2017)[12] histopathological correlations were available in 39 cases with 11 cases being the malignant lesions. Cyto-histological type agreement rate of 84% was observed in Pujani et al (2018)[8], 30% reported by Mihashi et al (2006)[13], Jain et al. (2013)[14] observed a cyto-histo correlation in 64.2% of malignant tumors.

Analysis of the 58 cases revealed that 9 cases were identified as malignant (true positive) out of 14 malignant cases identified by histopathological diagnosis. The sensitivity of the cytopathological diagnosis was 64.29%, specificity was 95.45%, positive predictive value was 81.82%, and negative predictive value was 89.36, and accuracy was 87.93%, our findings were in correspondence with other studies too.

Kakoty S et al (2017)[12] the specificity and the sensitivity were found to be 96.42% and 90.91% respectively. The predictive value of salivary gland cytology was 90.91% and diagnostic accuracy was 94.87%. Fine Needle Aspiration Cytology is thus a safe, reliable, quick, convenient and accurate method of diagnosis and should be considered as one of the first line of investigations in the evaluation of salivary gland lesions.

Conclusion

FNAC as a safe, simple, rapid, reliable, cost-effective, and well tolerated preoperative procedure with minimal morbidity carried out in outpatient department yielding accurate

diagnosis of inflammatory, benign, and malignant salivary gland lesions with good sensitivity and specificity.FNAC can be used preoperatively to avoid unnecessary surgeries and the discomfort to open biopsy. It is preferred over biopsies for salivary gland lesions as it is easily accessible, chances of spillage, recurrence and capsular infiltration are minimal. FNAC for palpable salivary gland lesions is a diagnostic and therapeutic asset. One of the limitations of our study is its small sample size.

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