RESEARCH ARTICLE

Diagnostic accuracy of fine needle aspiration cytology in comparison to open biopsy for lesions of oral cavity in COVID-19 era

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Abstract

Objective: To compare the diagnostic accuracy and uses of fine needle aspiration cytology with histopathology in the diagnosis of lesions of oral cavity.

Method: The single-centre, prospective, non-randomised controlled trial was conducted at the departments of Oral and Maxillofacial Surgery and Pathology of Allama Iqbal Medical College/Jinnah Hospital, Lahore, Pakistan, from January 10 to August 10, 2021, and comprised patients of either gender aged >10 years having superficial or deep well-established mass, palpable, nodular, ulcerative lesions, swellings of the oral cavity or of major or minor salivary glands having intraoral presence or manifestation with size >1 cm. Data was analysed using SPSS 20.

Results: Of the 43 patients, 22(51.2%) were males and 21(48.8%) were females. The overall mean age was 40.5±15 years (range 13-70 years). On cytological examination, 6(14%) samples were excluded for being insufficient aspirate. Of the remaining 37(86%) samples, 20(51.4%) were detected with malignancy on histopathology. The accuracy of fine needle aspiration cytology was 33(89.19%).

Conclusion: Fine needle aspiration was found to be a reliable and cost-effective technique in the diagnosis of oral cavity lesions.

Keywords: Carcinoma, Squamous cell, Fine-needle, COVID-19, Minimally invasive surgical procedures, Mouth neoplasms.

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Introduction

The term biopsy has its origin from the Greek words 'bios', meaning life, and 'opsis', meaning a sight. It was first conceived in 1879.[1] It involves the removal of a small piece of a tissue from the body of a living organism to examine it under the microscope or some form of magnification.[1] But the history of the origin of the technique in literature dates back to the 10th century when Arab physician Abulcasis (1013-1107) used a needle puncture on thyroid to differentiate between various forms of goiter.[1] The modern way of removing the tissue by aspiration by using fine needles is attributed to Martin and Ellis who founded this method in early 20th century.[1] In the later part of the same century, the Swedish School of Cytopathology embraced this technique and extended to the world.[1] There are various ways to perform these biopsies. A sharp instrument or surgical knife is used to remove the piece of the tissue, or it is done by using fine bore needles to aspirate the tissue or cells.[2] The procedure can be guided by ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI).[2]

The diagnosis of several oral diseases and conditions relies on removal of the tissue for histopathological examination.[3-5] Incisional or excisional biopsy for the purpose of definite diagnosis are considered the gold standard.[3,4] But the drawback is that it causes a lot of discomfort to the patient and may produce unwanted bleeding due to the vascularity of the oral mucosa.[3,4] It is also a more invasive method requiring time to perform.[3,4] There is a significant difference in the cost and processing time when compared to a fine needle aspiration cytology (FNAC),[3-5] resulting in delays in the planning of definitive treatment.[3,4] It is very important to select the most appropriate site for the biopsy and requires proper skills to perform the procedure in the oral cavity.[3,4] When the lesions are large and located in areas with poor accessibility, surgeons face difficulties in collecting the most appropriate specimen.[3,4] Moreover, sometimes a diagnostician is also reluctant to interrupt an encapsulated tumour to prevent an extra-capsular spread.[3,4] There are cases where it is not possible to even carry out biopsy as the patients may be medically compromised, using anticoagulants, or have limited mouth opening that limits the access.[3,4] Also, some patients with asymptomatic lesion may not give their consent for biopsy.[3,4] There are times when patient needs to be hospitalised before or after the procedure, and subsequent emergency visits with complaints of bleeding from the biopsy site is a routine experience.[3,4] The high patient turnover in the public facilities of developing and under-developed countries

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causes delays in getting an appointment for biopsy and then in reporting of histopathological diagnosis, which allows the disease to progress to a more advanced stage, and even increasing morbidity and mortality in patients.[3,4,6] Considering the simplicity and rapidity of fine needle aspiration cytology (FNAC), it is considered a very safe and minimally invasive procedure.[2-5,7] It can also be done on an outpatient basis, or in an ambulatory setting with very little preparation and equipment.[2-4] It is commonly used as a diagnostic modality in the diseases of the salivary glands and in the diagnosis of lumps in the body, including the head and neck region.[3,4,7] But the technique is not a common practice for the diagnosis of lesions of oral cavity, where biopsy and histopathological diagnosis is the gold standard.[3,4,7] It could be because of inexperience, variation or heterogeneity in the nature of lesions with respect to their anatomic locations, and the inconvenience in fixing the lesion for aspiration.[3,4] There are very few studies available correlating the accuracy of cytological diagnosis with the histological one using FNAC and incisional or excisional biopsy for the lesions of oral cavity.[4,7] They have advocated that FNAC can be used as an alternative procedure.[4,5,7]

The coronavirus disease-2019 (COVID-19) has increased the risk of contracting the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) among oral and maxillofacial surgeons as the specialty deals in the region where the viral load is significant.[8] Removal of a specimen along with the achievement of haemostasis requires time and is a hazard for operating surgeons and their teams. When FNAC is compared with open biopsy, it takes less time and minimal aerosol generation.[3,4] It can also be performed in patients where access to lesion is difficult and there is less chances of postoperative bleeding and pain.[2-4] The cost of the FNAC procedure is significantly low compared to a biopsy.[2-4] If the accuracy mentioned in other studies is considered acceptable, the use of the technique on an emergency basis to evaluate and diagnose cases of malignancy or oral pathologies requiring management should be a priority.[3,4] Another advantage is that it can be performed quickly with less exposure time for the surgeons and least discomforting to the patients with low cost and burden on any country with a struggling healthcare system.[3,4,8]

The current study was planned to compare the diagnostic accuracy and uses of FNAC with histopathology in the diagnosis of lesions of oral cavity. It was hypothesised that FNAC will fail to accurately diagnose lesions of oral cavity when compared to histopathological diagnosis.

Patients and Methods

The single-centre, prospective, non-randomised controlled trial was conducted at the departments of Oral and Maxillofacial Surgery and Pathology of Allama Iqbal Medical College/Jinnah Hospital, Lahore, Pakistan, from January 10 to August 10, 2021. The sample was raised using non-probability purposive sampling technique. The patients were enrolled from the outpatient department (OPD) of Jinnah Hospital, Lahore, after sample size was calculated using confidence level of 95% and margin of error 5%. Those included were patients of either gender aged >10 years having superficial or deep well-established mass, palpable, nodular, ulcerative lesions, swellings of the oral cavity or of major or minor salivary glands having intraoral presence or manifestation with size >1cm, and having no contraindications for performing fine-needle aspiration or an excisional or incisional biopsy.[3,4] Those excluded were pregnant women, children age 10 years or below, patients with the bleeding disorders or on anticoagulant therapy.[3,4] Patients who refused to participate or were uncooperative were also excluded, and so were those with superficial flat lesions, like macules, papules, port-wine lesions and vascular lesions.

Approval was obtained from the institutional ethics review committee, and informed consent was taken from all the participants. All demographic details and data of detailed clinical examination were collected. Bias and confounders were controlled by exclusion criteria. All baseline investigations were done for surgical procedure, including reverse transcription polymerase chain reaction (RT-PCR) for COVID-19.[9] Clinically, swellings, exophytic growths and lesions were examined and findings were documented.[3,4] Samples were collected using intraoral approach.[3,4,5] Slides were marked by patient name and identification number. FNAC was performed by disinfecting the oral cavity by using chlorhexidine gluconate 0.12-0.2% oral rinses commercially available.[10] A 22-23 gauge needle connected to a 5cc disposable plastic syringe was used for all needle aspirations.[3,4] Using the thumb and the index finger, the desired area from where the aspiration was planned to be taken was immobilised when it was necessary.[3,4] The needle was inserted without the use of any local anaesthesia into the mass or lesion with the single and slow motion without any negative pressure.[3,4] When the needle was inside the targeted area, negative pressure in the syringe was generated that helped in withdrawal of the material into the needle. The needle was moved a few times in a back and forth motion and in different directions within the localised lesion or mass. The negative pressure on the syringe was released before the needle was withdrawn. This reduced the chance of seeding the path of syringe with the aspirated cells and also to prevent aspiration of cells from healthy area or area not under consideration. The aspirate was forced out on to the slides,

and smears were prepared. Standard cytological staining techniques were used and the slides were inspected by two double-blinded pathologists. The cytological aspirates were broadly classified as adequate or inadequate, depending on the amount of material aspirated. Adequate specimens were further classified and sub-classified as neoplastic (benign, atypical cells, suspicion of malignancy, malignant) and non-neoplastic.[3,4]

For the purpose of analysis, atypical cells were considered negative, and suspicion of malignancy or where pathologist expressed suspicion for a diagnosis or malignancy was considered positive. The samples in which the aspirated material was insufficient or only the blood was present were considered inadequate and they were excluded from the final analysis.[3,4]

For excisional or incisional biopsy, the relevant procedure was performed and the specimen was fixed in 10% formalin solution and evaluated by the standard histopathological tissue examination techniques. Histopathological report was the gold standard against which cytological results were compared.[3,4]

In some patients, minor complications, like gag reflex, were observed and managed. Haemostasis was achieved before discharging the patient in a vitally stable state with proper verbal and written instructions.

The researchers wore proper and recommended personal protective equipment (PPE) along with N95 masks and eye protection to prevent themselves from SARS-CoV-2.[8,9] The procedure was conducted in a well-ventilated room with minimal use of oral suctioning to avoid excessive aerosol generation.[8,9] The contact or working time was kept to the minimum, but necessary to ensure safety of the operator along with proper completion of the procedure.[8]

Data was analysed using SPSS 20. Qualitative variables were presented as frequencies and percentages.

Results

Of the 43 patients, 22(51.2%) were males and 21(48.8%) were females. The overall mean age was 40.5±15 years (range 13-70 years). Mandible was the most common location from where the specimen were collected 11(25.6%) (Table 1).

Table-1: Intra-oral locations from where the specimen were collected.

Site	n (%)
Mandible	11 (25.6)
Maxilla	10 (23.3)
Buccal Mucosa	8 (18.6)
Tongue	6 (14)
Lip	4 (9.3)
Palate	2 (4.6)
Floor of the mouth	2 (4.6)
Total	43 (100)

Table-2: Comparison between histological and cytological diagnosis and distribution according to the nature of the lesion.

Histological Diagnosis	n (%)	Cytological Diagnosis	
		Consonant	Dissonant
Squamous Cell Carcinoma	18(48.64)	16	2
Inflammation	4(10.81)	4	0
Pleomorphic adenoma	2(5.41)	2	0
Fibrous hyperplasia	2(5.41)	2	0
Oral Aspergillosis	2(5.41)	2	0
Ameloblastoma	2(5.41)	2	0
Pyogenic granuloma	2(5.41)	1	1
Mucoepidermoid carcinoma	1(2.7)	0	1
Warthin tumour	1(2.7)	1	0
Salivary duct carcinoma	1(2.7)	1	0
Chronic sialadenitis	1(2.7)	1	0
Mucormycosis	1(2.7)	1	0
Total	37(100)	33	4

Table-3: Study outcome.

Nature of Lesion			Accuracy	Sensitivity	Specificity
Neoplastic 29 (78.4%)	Benign 9 (24.3%)		88.89%	88.89%	100%
	Malignant 20 (54.1%)	n=20	85%	89.47%	94.4%
		Squamous Cell Carcinoma 18 (90%)	88.89%	88.89%	100%
Non-Neoplastic 8 (21.6%)			100%	100%	100%
Total=37			89.19%	91.67%	97.06%

On cytological examination, 6(14%) samples were excluded for being insufficient aspirate. Only 4(10.8%) FNAC samples had incongruous in relation to histopathology (Table 2), showing FNAC accuracy 89.19%, sensitivity 91.67% and specificity 97.06% (Table 3).

Discussion

The study showed that the accuracy of FNAC was 89.19%, sensitivity was 91.67% and specificity was 97.06%. Some previously conducted studies had their results for the accuracy ranging from 79% to 97% and in some studies 100% accuracy in diagnosing or differentiating between various oral benign and malignant lesions was found.[3-5,7] They also suggested that when the aspirates are enough, one can even correctly diagnose the pathology.[3,4,7] More than half (54.1%) of specimen were of malignant lesions predominantly squamous cell carcinoma.[3,4] The significant percentage of squamous cell carcinoma was also observed in other studies which might be due to its high prevalence.[6] Around 657,000 new cases of oral cancers are diagnosed every year around the world and the majority of them are from south and central Asian countries, including Pakistan where it is the second most common cancer and accounts

Figure-1: : Clinical presentation of an oral lesion.

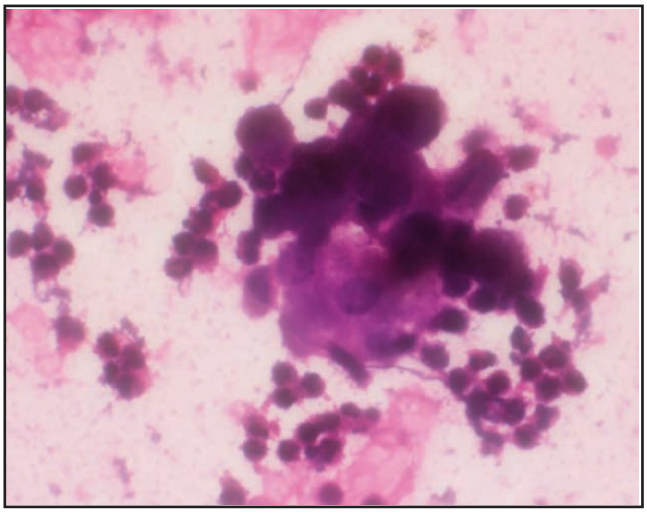

Figure-2: Malignant squamous cells in cytology smears with haemotoxylin and eosin (H&E) staining (40X).

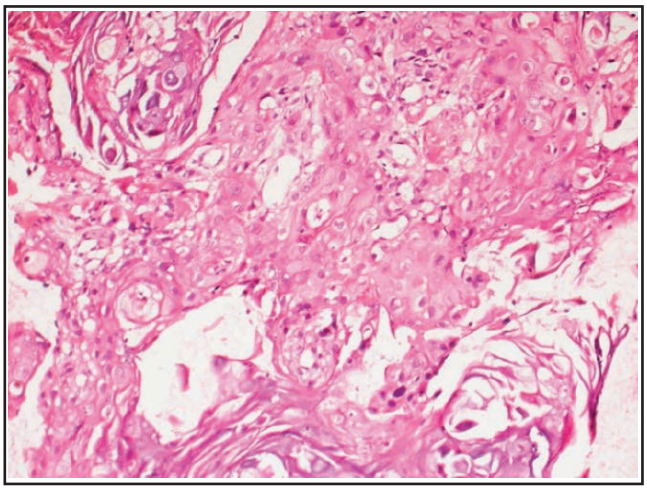

Figure-3: Histology of squamous cell carcinoma grade II with haemotoxylin and eosin (H&E) staining (40X).

for 10.9% of all the new cancers and 11.3% of cancer-related deaths.[11]

The current results validate earlier results.[3-5,7] The oral lesions and pathologies are as diverse as the oral cavity itself.[3,4] Proper diagnosis relies on good history, clinical examination and proper investigations.[3,4] Among the variety of investigations available, histopathological examination is considered the gold standard for definitive diagnosis.[3,4] The most commonly used method is incisional/ excisional or open biopsy for oral lesions, ulcers or masses.[3,4] The procedure is technique-sensitive, requires local anaesthesia and needs good patient cooperation.[3,4] For the preparation of histological slides, there are five basic steps involved; fixation, histoprocessing, embedding, sectioning and staining. The time required for these steps results in delayed final reporting of histopathology results. The cost of procedure and reporting is sometimes beyond the affordability of many patients, especially in poor and developing countries.[3,4] The dilemma of such countries is that the oral pathologies and conditions are highly prevalent due to poor socioeconomic conditions of the masses, poor oral hygiene and lack of proper awareness.[5,6,8] The healthcare system is also quite weak and is not enough to accommodate the increasing needs of the population.[8] Various habits, diets, misconceptions and myths among majorly illiterate societies and communities further add to the problems of delays or reluctances to timely seek expert guidance or help, with the net outcome of increase in morbidity and mortality of the patients.[3,4,6,8,12,13] Sometimes the very minor oral condition or disease turn into a life-threatening conditions or situations.[3,12,13] Delays could be sometimes due to the limited facilities available, overrun by patients more than their capacities.[6] Setting patient appointments for biopsy involves delays as the procedure requires special setting, skills and equipment.[3,4]

The COVID-19 pandemic further escalated the problem as it spread by aerosol, and oral cavity and its vicinity carry high viral load, exposing the surgeons to the risk of contracting SARS-CoV-2.[8,9] Procedures like biopsy require time, use of electric cautery and also cause aerosol generation. To minimize the risk of the virus and efficiently manage and diagnose the increasing number of patients, alternative techniques need to be explored.[3,4] The ideal technique or procedure is the one that requires low level of skill, is reliable and cost-effective, can be quickly performed in an ambulatory setting, needs less contact time with the patient, cause less aerosol generation and have a short reporting time.[3-5] One of such procedures is FNAC, which has many of these advantages.[3,4] In case of biopsy, sometimes it is very important to take a proper

sample in the first go because of the irreversible damage the procedure causes to the tissue.[3,4] With fine needle aspiration, one can also repeat the procedure if the aspirates collected are not enough.[3,4] On average, FNAC requires from a few seconds to <5 minutes to perform, while biopsy can take 15-60 minutes. It takes a few hours to a maximum of 48 hours to report cytology results, while a histopathology report can take 7-14 days. The use of FNAC in the diagnosis of the salivary gland pathologies is very common and very well established.[3,4,7] But FNAC is not commonly used for the diagnosis of lesions and masses of the oral cavity, such as squamous cell carcinoma, where histopathology is the gold standard.[3,4,7] In the light of the findings, it is FNAC seems to be good enough for use as a regular or emergency procedure in separating the malignant lesions from the benign ones, and non-neoplastic pathologies from the neoplastic ones, especially when limitation of resources in proportion to number of patients is an important concern, or there is respiratory pandemic situation.[3,4,8] It can help in early and timely management of malignant lesions or masses from the benign ones.[3,4,12] In case of some non-neoplastic pathologies, early and quick diagnosis can help in the timely management without wasting time on a surgical procedure.[3,4,7,12]

The current study had some limitations, like a small sample size, which was enough from the statistical point of view.[3,4] A larger sample size would have given a better insight or accurate results. The samples were collected in the procedure room and were transported to the pathologist. The unavailability of light microscopy and pathologist in the procedure room when the samples were being collected resulted in some samples having insufficient material for cytology which later had to be excluded. There was no repeat sampling, and no immediate examination of samples using microscopy for blood or insufficient material. To collect good sample, immobilisation was necessary.[3,4] Immobilisation of the area of interest was difficult in some cases while collecting the aspirates which affected the amount of material collected and could have also impacted the results. Sufficient quantity of material would have given more accurate results.[3,4] It is important to observe caution while immobilizing the tongue or soft tissue using fingers while trying to get good sample as the risk of needle prick is high while collecting cytological aspirates. Some of the current limitations were common with earlier studies.[3,4]

Conclusion

Fine needle aspiration was found to be a very rapid, reliable, cost-effective procedure. It can be deployed for regular or emergency purposes to differentiate between various benign and malignant pathologies, and also between neoplastic and non-neoplastic ones. It can be helpful and a repurposed tool in the armamentarium of oral surgeons during the COVID-19 or other respiratory pandemics.

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