

**CORRELATION OF BRUSH CYTOLOGY AND IMPRINT CYTOLOGY WITH
HISTOPATHOLOGY IN UPPER GASTROINTESTINAL LESIONS**Dr. Prachi Singh¹, Dr. Faiyaz Ahmad^{2*}, Dr. Shyamoli Dutta³, Dr. Seema Awasthi⁴ and Dr. V. K. Singh⁵¹Post Graduate Student, Department of Pathology TMMC&RC, Moradabad, Uttar Pradesh.^{2,3}MD, Professor, Department of Pathology TMMC&RC, Moradabad, Uttar Pradesh.⁴MD, Professor and Head, Department of Pathology TMMC&RC, Moradabad, Uttar Pradesh.⁵MD, Professor and Head Department of Internal Medicine TMMC&RC, Moradabad, Uttar Pradesh.***Corresponding Author: Dr. Faiyaz Ahmad**

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ABSTRACT

Background: Various pathologies can affect upper gastro intestinal tract. Malignancies are not uncommon and early diagnosis have excellent outcomes. Endoscopic brush cytology has sensitivity and specificity between 90%-96%. Imprint cytology is a rapid tool with sensitivity and specificity about 95%-100%. Histopathology is gold standard, but is time consuming compared to cytology. **Objectives:** Correlation of brush cytology, imprint cytology and standard histopathology of upper gastrointestinal tract lesions. **Material and methods:** 50 patients with upper gastrointestinal tract lesions were included. cytological brushing done from lesions. Biopsies were taken and the imprint smears were then made. Diagnoses were made on brush smears, imprint smears and histopathological sections separately. **Results:** Patients were between 20-85 years. Lesions of esophagus sampled (44.0%), gastric (40.0%) and duodenum (16.0%). **Conclusions:** Our study concludes that cyto-morphology can play a prominent diagnostic and prognostic role in evaluating digestive tract cancers. Touch smear cytology is efficient and reliable for immediate detection of upper gastrointestinal diseases.

KEYWORDS: Histopathology, imprint cytology, brush cytology.**INTRODUCTION**

The "gastrointestinal tract" is defined as sequence of tubular organs along with accessory structures which are meant for digestion, absorption, assimilation of food and further removal of waste material. It is anatomically and physiologically subdivided into an upper digestive tract and lower tract and various accessory organs.^[1]

There is a wide range of pathologies affecting upper GIT like infectious diseases, inflammatory disorders, mechanical, toxic and physical agents including radiation injury and neoplasms.^[2]

Digestive tract cancer is one of the most common malignancies in humans and is amongst the leading causes of death. Early stage cancer is asymptomatic and curable.^[3]

India is also experiencing a simultaneous increase in cancer cases with increased detection rates and advancement in cancer care. In 2018 over 1.1 million new cancer patients were registered in India and 0.78 million people died of cancer.^[4]

Oesophageal cancer: In India, it is the fourth most common cause of cancer associated deaths. Presently

Squamous cell carcinoma is the commonest type of esophageal cancer in the Indian subcontinent and the most common portion involved is the distal third of the esophagus.^[5]

Stomach cancer- Cancers located at cardia and non-cardia are important cancer worldwide and were responsible for more than 10 lakh new cases in year 2018 with a total number of 783,000 deaths, makes it the 5th frequently diagnosed malignancy and the third leading cause of cancer associated deaths.^[6]

Small intestine cancers- Are comparatively rarely seen, comprising total 2% of all gastrointestinal cancers in the US. Among small gut neoplasms majority of cancers originate from the ileum, after which comes duodenum and least commonly involved is jejunum. While in the ileum tumours are mostly of neuroendocrine type, adenocarcinoma is the main type of duodenum malignancy.^[7]

Upper digestive tract pathologies: changing scenario in India

India is one of developing nation with one of the most diverse populations and dietary habits globally. Digestive tract related ailments in India are increasingly being

reported because of increasing migration of rural population to big cities and with change in way of living.

The common implications for UGIE are difficulty in deglutition, dyspepsia, continuous heartburn, constant nausea and emesis, upper GI hemorrhage/ anemia, non-responsiveness of symptoms to H2 antagonists and PPIs, unusual chest pain, marked weight reduction and follow-up screening of known cases of Barrett's esophagitis or lesions.

Any type of physical or physiological trauma to the digestive tract can impair the ability to sense and abandon injurious substances exposed to the alimentary tract, thus leading to cell and genetic material damage. This feature is associated with all chronic conditions including those which lead to neoplasms in the GI-tract.^[8]

The emergence of endoscopy and endoscopic biopsy has greatly facilitated the detection and diagnosis of gastrointestinal pathologies.^[9]

The simplicity, convenience and safety of modern endoscopy has resulted in major advances in managing lesions of GIT.^[10]

Since the introduction of image guided brush cytology in the mid 1970s, the utilization of this technique has proliferated which retrieves epithelial cells from a wider surface area of mucosa than that in a tissue biopsy. So, at present it is the most frequently performed procedure in interventional radiology.^[3]

Imprint cytology is a major breakthrough in the field of rapid tissue diagnosis. Besides its speed and enormous simplicity, it provides excellent cytological details.^[11]

Endoscopic biopsy is an essential part of the evaluation of GI pathology. In the diagnosis of upper GI lesions, histopathological evaluation is considered gold standard but is very time taking, compared to cytology.^[12]

Lots of literature is available on the efficacy and correlation of brush cytology and imprint cytology with histopathology. But very scant literature is available for the establishment of accuracy and correlation of all three diagnostic modalities.

MATERIALS AND METHODS

Settings: This study was conducted in the Department of Pathology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh (India).

Duration: July 2018 to December 2019.

Type of study: Prospective and observational.

Sample size: A total of 50 patients with neoplastic and non-neoplastic upper GI lesions were included in the study.

Inclusion criteria: Patients presented with upper GI symptoms such as- Dysphagia, vomiting, retrosternal pain, anorexia, loss of weight, mass abdomen and Patients with visible erythematous lesions, ulcers, polypoidal or ulcerative growth in upper GIT on endoscopy.

Exclusion criteria: Patients not fit for upper GI endoscopy, patients with oral lesions only, radiologically extensive lesions, biopsies with inadequate material and slides showing crush artifacts were excluded.

Sampling method: Endoscopy was done by using fiber-optic video endoscope. Patients with visible mucosal lesions in the upper GIT were included.

After visual examination of the lesion, a cytological brush was introduced through a separate channel in the endoscope and advanced to the lesion obtained by leading the brush several times across the lesion until mucosal bleeding was observed.

After withdrawing the brush, the material was smeared onto clean, dry, labelled glass slides with utmost care to obtain adequate and well preserved material. A minimum of 2 to a maximum of 4 smears were made with each brushing.

After brushing, biopsies were taken from suspicious area with help of biopsy forceps. The biopsy samples were transferred from the forceps to two slides with a fine needle, and the smears were then made by gently rotating the tissue with the needle. Both brush and imprint smears were fixed in 95% ethyl alcohol and stained with H&E stain, 2-3 smears of each kept air dried for Romanowsky staining.

The same tissue after imprint smear preparation was collected for histopathological examination. Tissue was transferred to a bottle containing 10% formalin with proper tagging and was kept for overnight fixation. Routine tissue processing with paraffin impregnation was done and sections were stained with H&E.

The diagnosis of upper gastrointestinal tract lesions was made on brush smears, imprint smears and histopathological sections separately according to the cytopathological and histopathological findings. Typing & grading of malignant lesions on histopathology was done according to WHO classification.

Data collection procedure and analysis: All the relevant clinical details including the age, sex, clinical presentation, endoscopic findings and the clinical diagnosis of the patients were noted. Details of procedure were explained to each patient and the consent (written

in patient's own language) was obtained before the procedure.

Ethical consideration: Ethical clearance was received from the institutional Ethical committee before conducting the study.

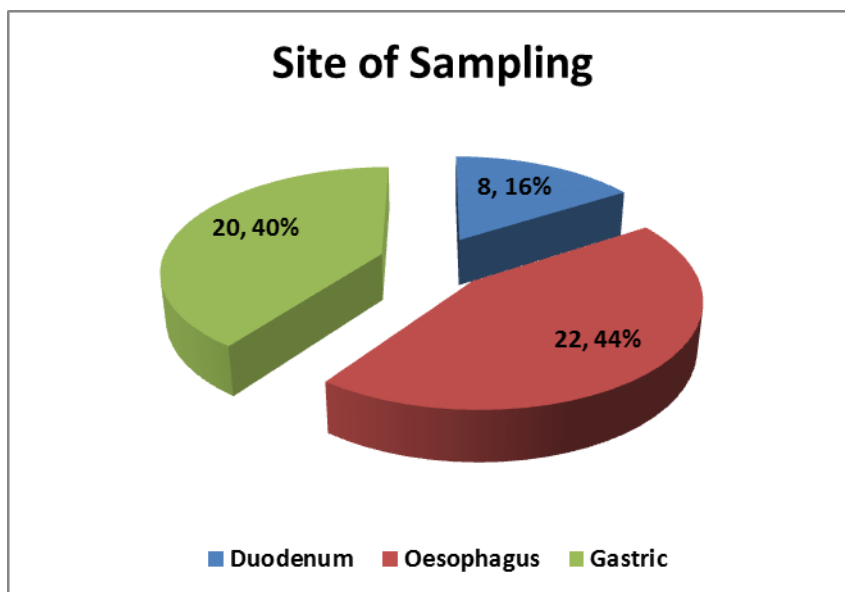
RESULTS

Table-1: Age range and mean age of study population.

	Minimum	Maximum	Mean	Std. Deviation
Age	20.00	85.00	49.64	15.81

Table-2: Distribution of UGI lesions according to site of sampling.

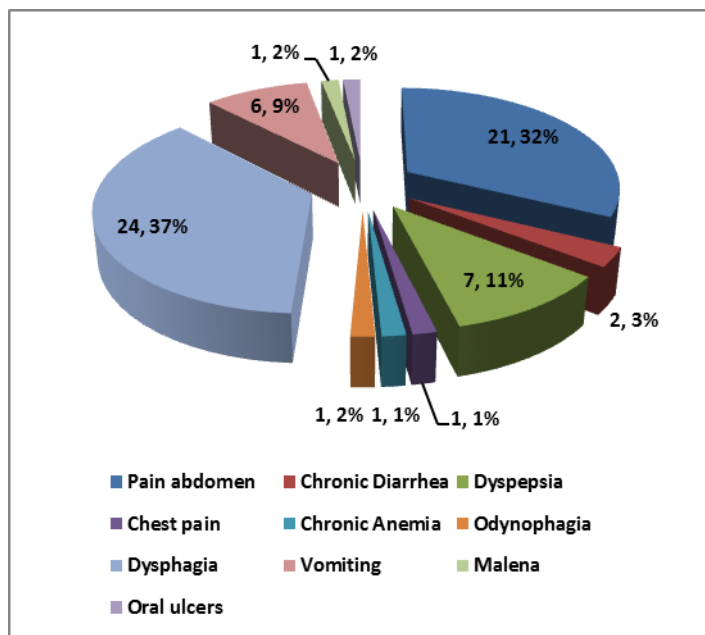
Site of Sampling	Frequency	Percent
Duodenum	8	16.0%
Oesophagus	22	44.0%
Gastric	20	40.0%
Total	50	100.0%



Pie chart-1: Distribution of lesions based on site involved.

Table 3: Frequency of presenting symptoms in UGI lesions.

	Frequency	Percent
Pain abdomen	21	42.0%
Chronic Diarrhea	2	4.0%
Dyspepsia	7	14.0%
Chest pain	1	2.0%
Chronic Anemia	1	2.0%
Odynophagia	1	2.0%
Dysphagia	24	48.0%
Vomiting	6	12.0%
Malena	1	2.0%
Oral ulcers	1	2.0%



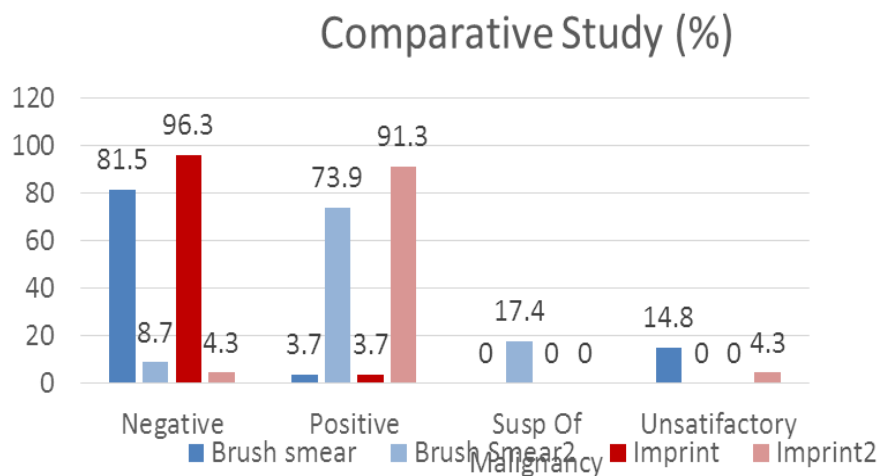
Pie chart-2: Distribution of presenting symptoms in patients with upper GI lesions.

Table-4: Sensitivity and specificity of brush cytology.

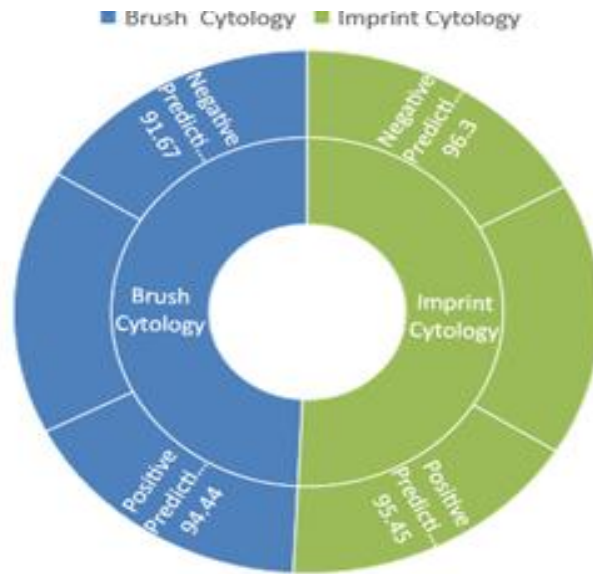
Brush Cytology	Predicted Y	Predicted N
Actual = Y	17	1
Actual = N	2	22

Table-5: Sensitivity and specificity of imprint cytology.

Imprint Cytology	Predicted Y	Predicted N
Actual = Y	21	1
Actual = N	1	26



Bar diagram-1: Comparison of histopathology with imprint smear and brush smear cytology.



Doughnut chart 1: Predictive values in brush and imprint cytology.

The sensitivity and specificity for

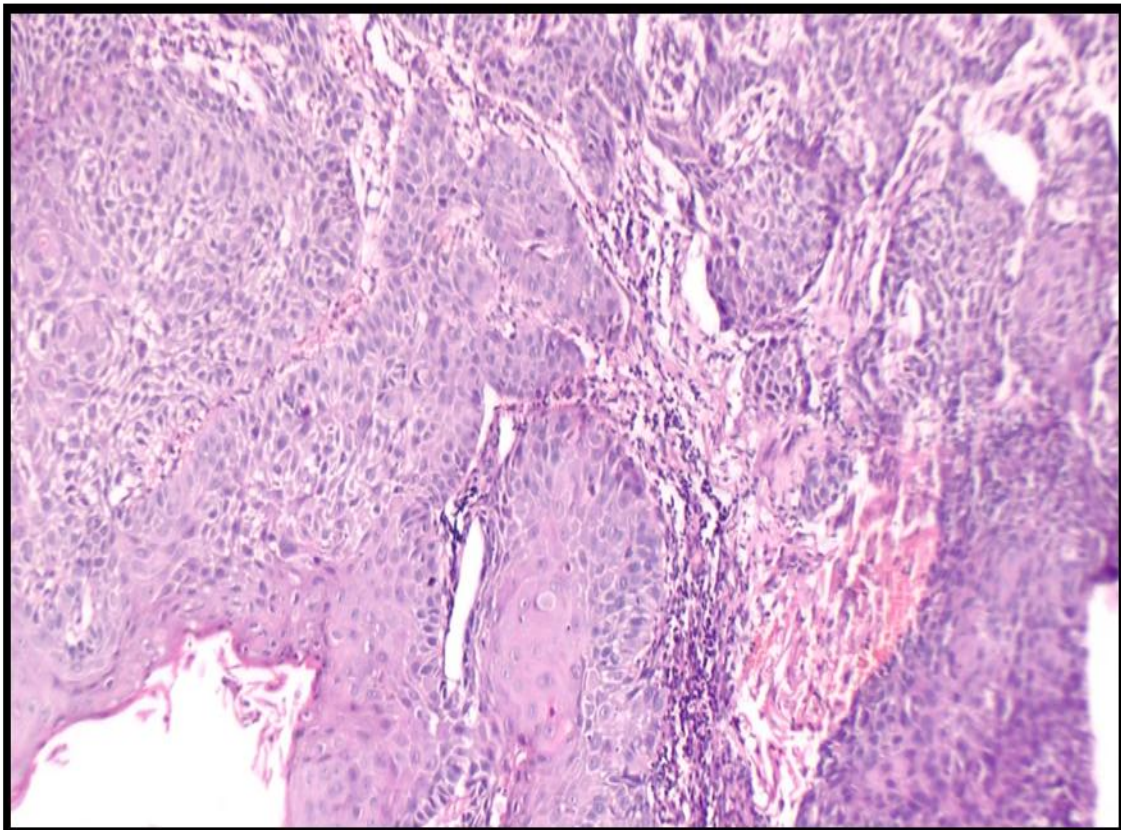
Brush cytology- 89.47% and 95.65%,
Imprint cytology-95.45%, and 96.30%

Positive and negative predictive values

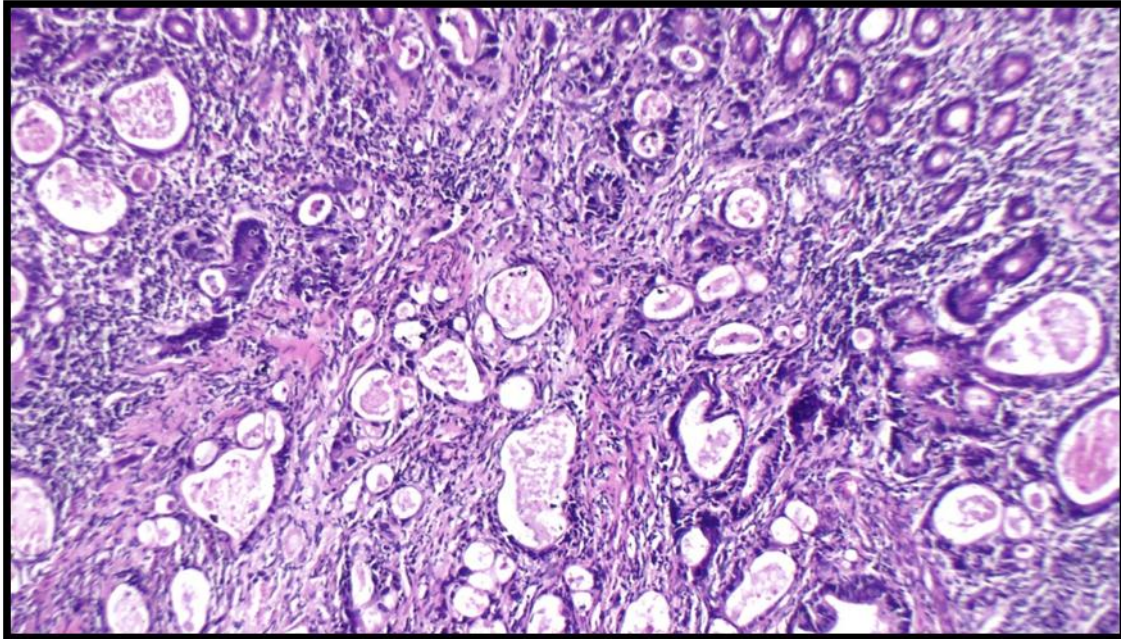
Brush cytology-94.44%, 91.67%,
Imprint cytology-95.45%, 96.30%

Diagnostic accuracy- 92.86% & 95.92% respectively.

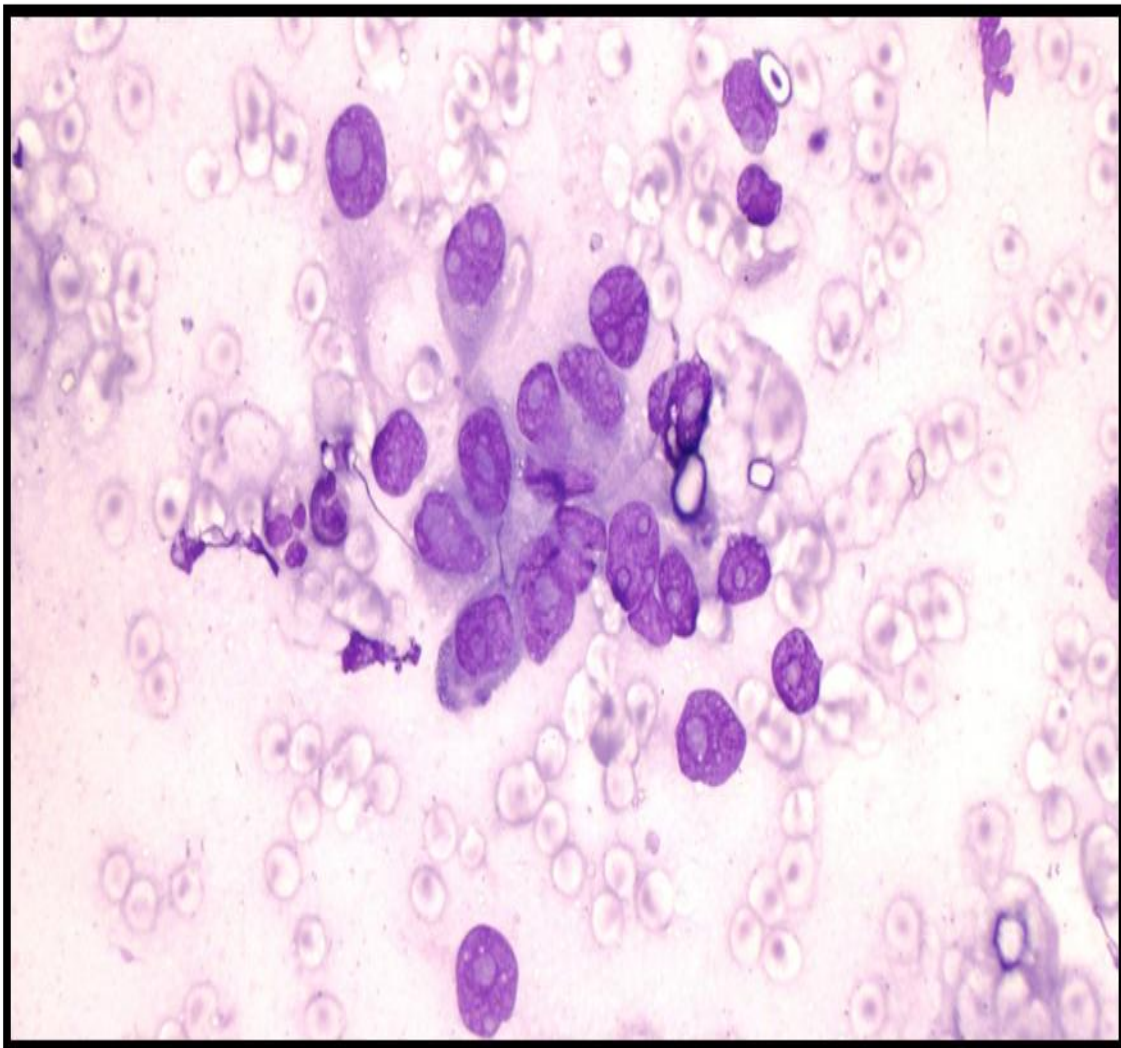
Photomicrograph 1: SQUAMOUS CELL CARCINOMA, ESOPHAGUS (200X, H&E)



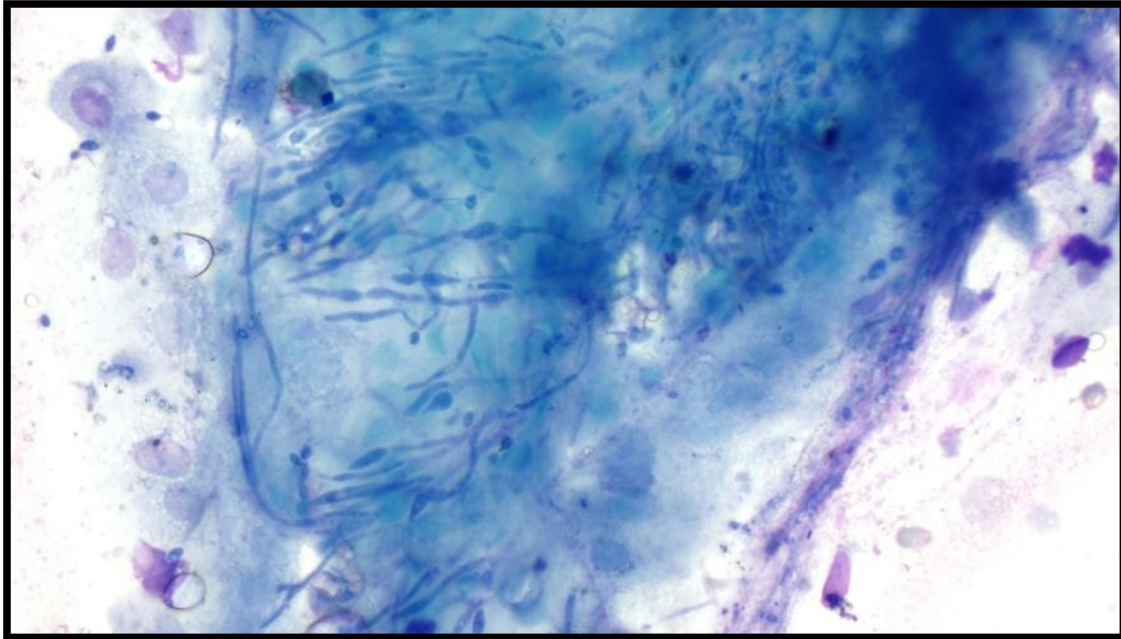
Photomicrograph 2: LOW GRADE ADENOCARCINOMA, DUODENUM (200X, H&E)



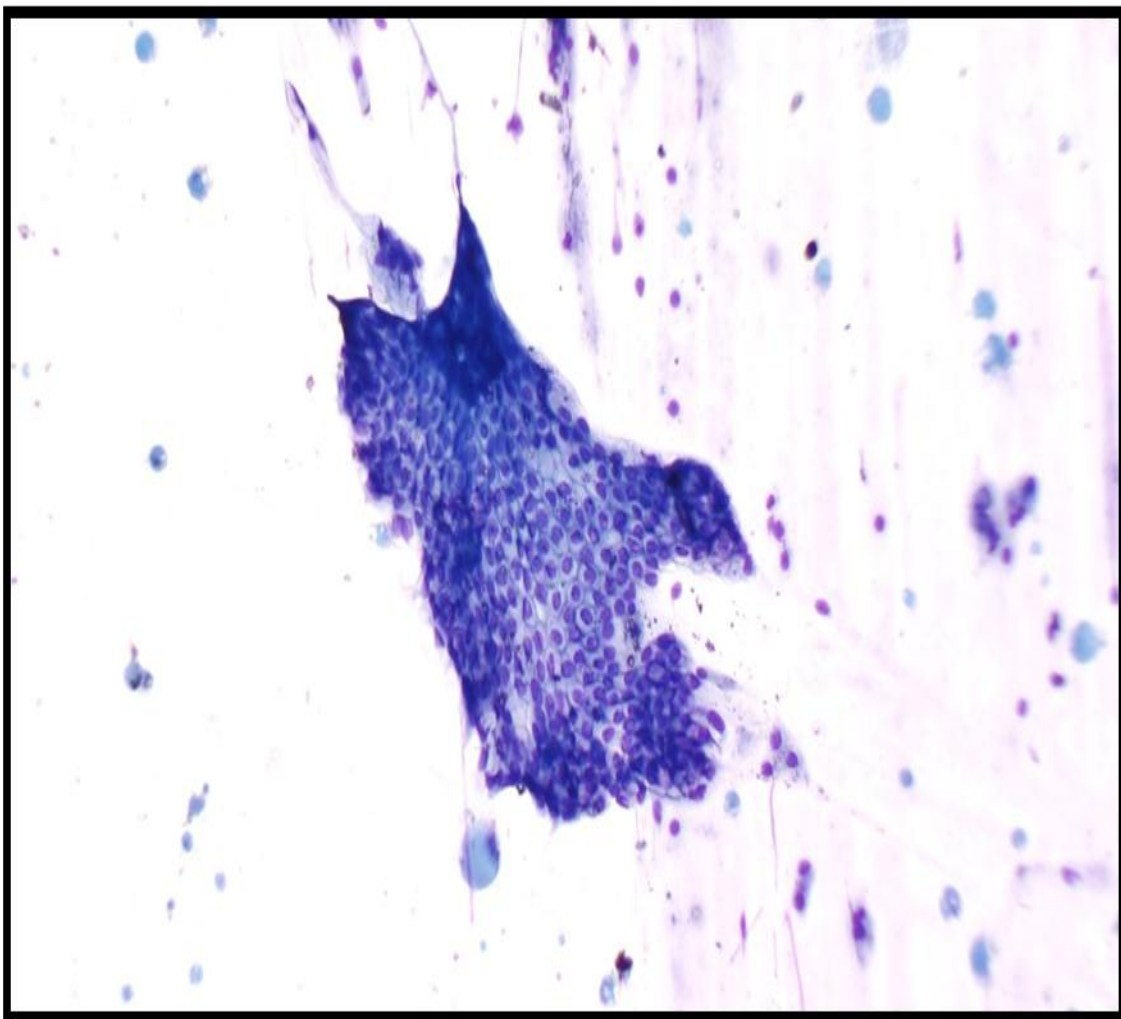
Photomicrograph 3: GASTRIC ADENOCARCINOMA (400X, MGG- IMPRINT SMEAR)

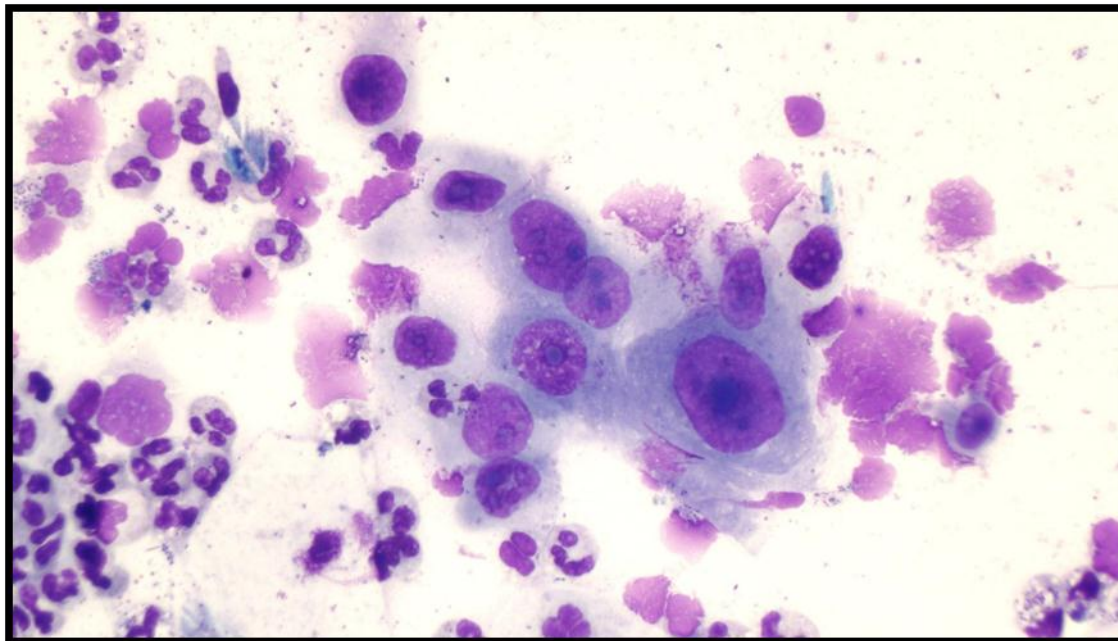


Photomicrograph 4: ESOPHAGEAL CANDIDIASIS (400X,PAS- BRUSH SMEAR)



Photomicrograph 5: MONOLAYERED SHEETS OF NORMAL EPITHELIAL CELLS (100X,MGG-BRUSH SMEAR)



Photomicrograph 6: SQUAMOUS CELL CARCINOMA (400X,MGG-IMPRINT SMEAR)

DISCUSSION

Diagnosis of digestive tract cancers is the main benefit of GI cytology. Its calibre, has been described in literature even before the discovery of upper GI endoscopy. The cytological specimens can be collected along with the histopathological sample under the guidance of endoscope which helps in examining exact site of mucosal lesions.

Admittedly oesophagogastric and colorectal malignancies are found to be most prevalent and frequently encountered cancers in humans.^[13] Gastric cancer is the 5th frequently diagnosed malignancy and the third leading cause of cancer associated deaths worldwide. In men rates are 2 times higher than that of women.^[6]

In our study 50 brushing and 50 imprint samples taken from 50 patients having upper gastrointestinal tract lesions were assessed to see the role of brush smear and imprint smear cytology in diagnosing various lesions occurring in the proximal GIT and to correlate both with endoscopic upper GI biopsy. The diagnosis on histopathology was considered as gold standard.

Age wise distribution of study population

The age range of the study population was 20-85 years with a mean age of 49.64 years. In present study majority of patients who underwent endoscopy guided brush and imprint cytology sampling, were of 50 or above 50 years of age with total (56%) cases.

These parameters resemble the results of study done by Kaur^[14] S and Keya^[13] et al. The mean age is comparable with study done by Vidyavathi^[9] and Vijayanarasimha D^[12] with an average age of 55 years.

Gender wise distribution of study population

In the present study gender ratio was 1.63 which is similar with study done by Keya^[13] et al where it was 1.33:1.

Gender and age distribution in malignant cases

This investigation found overall gender incidence of 1.1:1 for upper GI tract malignancies but in patients aged 50 years or above who were positive for malignancy, there was male predilection with a M:F ratio of 1.6:1, which is in concordance with that reported elsewhere in the world literature.

Present research had 1 patient who had been diagnosed to have carcinoma in her early thirties while 4 patients had carcinoma in their mid-forties.

As noted by various other authors SCC was the commonest malignancy of the oesophagus in the present study.^[15]

Clinical presentation

In this study majority of the patients presented with dysphagia followed by pain abdomen, dyspepsia and vomiting. Other symptoms were chronic diarrhoea, chest pain, chronic anemia, odynophagia and oral ulcers.

In the research by Keya^[13] et al clinical presentations of study patients were upper abdominal pain, dysphagia, vomiting, anorexia, distended abdomen and sometimes abdominal mass. Epigastric pain was the prominent symptom in case of gastric and duodenal lesions and dysphagia in case of oesophageal lesions.

Site of sampling

The frequent most site of sampling was found to be Oesophagus in 22 (44.0%), followed by stomach in 20

(40.0%) and least common was duodenum among 8 (16.0%) cases.

This was in discordance to the study by **Keya**^[13] and **Kaur**^[14] S where stomach was the most prevalent site of involvement followed by oesophagus.

Correlation of histopathology with brush cytology

In present assessment brush cytology found to be effective in confirming the diagnosis as malignancy in 17 patients, 22 cases were negative while 4 cases were reported as suspicious of malignancy. Total 4 cases were reported as inadequate or not suitable for opinion. The cases which were suspicious for malignancies on brush smears were positive for malignancy on histopathology in majority the site was oesophagus followed by stomach.

This was quite similar to the research conducted by **Chaudhary**^[16] and colleagues. In present investigation, the sensitivity of brush smear was 89.47%, specificity was 95.65%, positive predictive value was 94.44%, negative predictive value was 91.67% and diagnostic accuracy was 92.86%.

Vidyavathi^[9] in her study observed that sensitivity of brush cytology was 98.03% and specificity was 81.11%, which proved the utility of scrape cytology as a screening tool.

Shroff^[17] CP in his research obtained brush smear and endoscopic biopsy specimens from a total 4000 subjects presenting with upper digestive tract complaints over a period of five years. Cytology alone, could obtain a sensitivity of 79% and specificity of 98.5%.

Wang^[18] in his study concluded that combined use of GI cytology and histopathology increase the rate of pseudo positive cases, although it also increases overall sensitivity. In an investigation carried by **Donoghue**^[19] he found additional use of cytology, increased Sensitivity from (88.3 - 97.5) %. Hence cytology is suggested as an important adjunct tool in cases with doubtful mucosal sites. **Cook**^[20] and associates in their research found the sensitivity of combined cytology and biopsy to be 91%. As per authors, in situations when obtaining sufficient tissue for histopathology is difficult scrape cytology is an effective alternative.

The suspicious category in smear cytology prompts for possibility of a cancer and insists clinician for compulsory repeat sampling. Brushing cytology has many benefits as it is easily accepted by the subjects, penetrability to the basement membrane, easy access and collection of cells from all three epithelial layers as well as early detection of upper GI diseases. Cytobrush tends to cover a wider area of the lesion and hence recovers a better representative sample.^[21]

With the selection of appropriate site of sampling, sparing the lesions covered with necrotic material and competent and trained personnel for doing procedure diagnostic efficiency can be improved. Sample should be collected from the marginal zone of ulcer with a forceful stroke by proximal end of brush. Use of filter paper is required for soaking mucus and blood clot.

Correlation of histopathology with imprint cytology

With touch smear cytology use we can immediately assess whether the endoscopy guided histo-pathology sample is adequate or not.

Our observation and analysis found imprint smear cytology to be effective in confirming the diagnosis as malignancy in 21 patients. 1 case from oesophagus reported as inadequate or not suitable for opinion, while no case was reported as suspicious of malignancy. In current investigation, complete correlation between imprint cytological and histopathological diagnosis was obtained in 96.3% cases and there was 1 false negative case which clashes with the findings of **Keya**^[13] et al where complete correlation between imprint cytological and histopathological diagnosis was obtained in 94(94%) cases and 6 cases were misinterpreted on cytological examination.

In this study one false negative case was observed in gastric lesion.

This false negative result may be due to location of the lesion beneath the epithelium which missed on touch smear. False negative diagnosis in imprint cytology was also observed in sub-epithelial lesions studied by **Mahadevappa**^[10] A. In our analysis, the sensitivity of imprint smear was 95.45%, specificity was 96.30%, positive predictive value was 95.45%, negative predictive value was 96.30% and accuracy found to be 95.92%.

Comparable diagnostic statistics was observed in investigation by **Keya**^[13] et al, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of biopsy touch cytology in the diagnosis of upper digestive tract lesions were 98.46%, 91.42%, 95.52%, 96.97% and 96% respectively.

Sensitivity and specificity of IC recorded in various literatures range from 95% to-100%. Biopsy touch smear cytology was found to be at times better to biopsy in some investigations. The utility of touch cytology has been shown in the investigation by **Shaha**^[22] S and co-workers as compared to frozen sections. Where it was found to be equivalent with frozen sections in the diagnostic accuracy and sensitivity. This made them to conclude that imprint cytology can be used in place of frozen sections where frozen section can not be done.

The main drawback of cytopathology is its inability to differentiate between dysplasia or CIS from invasive

cancer. High cellularity with tumour cannibalism in cytology smear suggest invasion but not a sure sign of malignancy.^[21] Although GI histopathology is considered as confirmatory diagnostic test and is done on routine basis in all suspected alimentary tract pathologies but digesrtive tract cyto-smear study provides an efficient alternative tool if assessed with inclusion of 'suspicious for malignancy category'. It takes lesser time in examination, Patient discomfort is also very minimal.

Discordance of brush cytology with histopathology

4 cases were suspicious of malignancy on brush cytology, while positive on histopathology among these case site of sampling was oesophagus in 3 cases and stomach in 1 case.

1 case was found to be negative for malignancy on brush cytology while was positive for malignancy on histopathology, site of sampling was oesophagus. It may be due to difference in sampling site on catching the cells on brush.

2 cases were positive on brush smears were negative for malignancy on biopsy this is similar to study by Ricardo^[23] et al which had 5 false positive cases in their study. This may be due to slight difference in sampling site of brush and biopsy sample.

Yield of brush cytology

In our study the total number of brush smears obtained from a patient were between 2-4. Majority of smears were found to have adequate cellularity. In 4 cases smears were found unsatisfactory for opinion, among these in 3 smears there was sparse cellularity for any opinion while in 1 case dense inflammation was obscuring the native cells. The site of sampling in unsatisfactory smears were stomach in 3 cases and duodenum in 1 case. All cases on histopathological examination were found to be negative for malignancy.

Discordance of imprint cytology with histopathology

1 case from stomach found negative for malignancy on imprint smear was positive for malignancy on histopathology.

1 case from stomach found to be positive for malignancy on imprint was reported as hyperplastic epithelial polyp on histopathology.

Yield of imprint cytology

In our study the total number of imprint smears obtained from a patient were between 2-4. Majority of smears were found to have adequate cellularity. In 1 case from oesophagus smears were found unsatisfactory for opinion, because of inadequate cellularity.

CONCLUSION

- Cyto-morphology can play a prominent diagnostic and prognostic role in evaluating digestive tract

cancers, if it is dealt with competent approach regarding type and site of a GI tumor.

- The findings of the present investigation indicate that touch-smear cytology is reliable regarding immediate detection of upper GIT diseases, It is simple, accurate and cost effective.
- So, gastroenterologist or surgeon can take a therapeutic decision approximately one week earlier.
- Though imprint smears are accurate in identification of malignancy, they must be correlated with histopathology for assessing depth of invasion and for typing of tumors.

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