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Original Research Article

Cytological spectrum in patients of gastro-esophageal reflux disease: A prospective study in a tertiary care instituteShivani Sood^{*1}, Rajni Kaushik¹, Anchana Gulati¹, Brij Sharma², Pranav Sood³, Pooja Chauhan¹ and Ganga Rawat⁴¹Department of Pathology, Indira Gandhi Medical College, Shimla, HP, India²Department of Gastroenterology, Indira Gandhi Medical College, Shimla, HP, India³MD Gynaecology, M.O, Civil Hospital, Rohru, HP, India⁴DCP Pathology, DDU Hospital, Shimla, HP, India

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***Correspondence Info:**Dr. Shivani Sood
MD Pathology,
Senior Resident,
Department of Pathology,
Indira Gandhi Medical College, Shimla, HP, India***Article History:****Received:** 26/05/2017**Revised:** 11/06/2017**Accepted:** 11/06/2017**DOI:** <https://doi.org/10.7439/ijbr.v8i6.4185>**Abstract****Introduction:** Gastroesophageal reflux disease (GERD) is defined as reflux of gastric contents into mouth resulting in retrosternal burning sensation.**Aims:** This prospective study was undertaken with the aim to assess the cytological spectrum in esophageal brushings taken from patients with GERD and their correlation with esophageal biopsy.**Method:** Esophageal brushings and biopsies were taken from 150 patients of GERD and 50 controls. GERD cases were defined by the presence of classical symptoms of heart burn and/or acid regurgitation. Endoscopically, GERD cases were subdivided into erosive reflux disease (ERD) and non-erosive reflux disease (NERD). Three cytological parameters studied in esophageal brushings were reactive changes, presence or absence of inflammation and presence or absence of parabasal cells.**Results:** The most common finding was reactive changes with inflammation (56 cases, 37.33%) followed by inflammatory smears in 12 (8%) patients. Parabasal cells were not seen in any of the subjects with GERD. Presence of reactive changes with inflammation revealed a statistically significant correlation between GERD patients and controls ($p < 0.05$). However, the presence of inflammatory cells did not reveal a statistical significance. ($p = 0.136$). The sensitivity of cytology in our study was 68% and specificity was 95.12%.**Conclusion:** Cytology cannot be truly relied upon and can only be used as an adjunct to histopathology with both being complementary to each other.**Keywords:** GERD, esophageal brushings, reactive changes, inflammation.**1. Introduction**

Gastroesophageal reflux disease (GERD) is a chronic relapsing disorder characterized by reflux of gastric contents into the esophagus. Epidemiological data suggest that it is an emerging digestive disease in Asia and India as well.[1] A population based study in high altitude area in India also suggests a high prevalence (18.7%) of GERD.[2] It has received extensive attention during the past two

decades because it affects the quality of life of patients and imposes a large financial burden on the health care system.

Diagnosis of GERD is based on either the presence of classical symptoms (heartburn and/or reflux) associated with abnormal esophageal acid exposure or 24-hour pH monitoring and endoscopy along with esophageal biopsy.

On endoscopy, patients can be divided into non-erosive reflux disease (NERD) and erosive reflux disease

(ERD) depending upon the absence or presence of mucosal breaks. Esophageal brushings and biopsy samples can be obtained during endoscopy for cytological and histopathological examination respectively. The classical cytological changes in GERD are the presence of both reactive and degenerating squamous cells in the background of mixed inflammatory cells, predominantly composed of neutrophils.[3] This study has been undertaken to study the cytological changes in patients of GERD and to correlate cytologic findings with histologic findings.

2. Method

This prospective study was conducted for a period of one year on patients attending the department of gastroenterology with complaints of heartburn and/or regurgitation. 50 subjects with no complaints of heart burn/regurgitation with normal endoscopic findings were included as control. Endoscopic brushings and biopsy samples were collected from both cases and controls. Also, on the basis of presence/absence of erosion/ulcer on

endoscopy, cases were further subdivided into NERD (non-erosive reflux disease) and ERD (erosive reflux disease) group respectively. Giemsa stain was done on cytological samples and biopsy was processed and stained with hematoxylin and eosin stain. Epi info software was used for statistical assessment of these histological parameters.

3. Results

From table 1, it is clear that in the GERD group, the most common finding was reactive changes with inflammation (56 cases, 37.33%) followed by inflammatory smears in 12 (8%) patients. Parabasal cells were not seen in any of the subjects with GERD. Presence of reactive changes with inflammation revealed a statistically significant correlation between GERD patients and controls ($p < 0.05$).

However, the presence of only inflammatory cells did not reveal any statistically significant correlation between GERD cases and controls ($p = 0.136$).

Table 1: Comparison of cytological findings in GERD patients with controls

Cytological findings	GERD (n=150)		Controls (n=50)		P value (Fisher's exact test)
	No.	%	No.	%	
Normal	32	21.33	39	78	<0.05
Inflammatory	12	8	1	2	0.136
Reactive changes with inflammation	56	37.33	1	2	<0.05
Scant material	50	33.33	9	18	

Table 2: Comparison of cytological findings of NERD with ERD

Cytological findings	NERD (n=80)		ERD (n=70)		P value (Fisher's exact test)
	No.	%	No.	%	
Normal	24	30	8	11.43	0.0056
Inflammatory	9	11.25	3	4.28	0.1167
Reactive changes with inflammation	25	31.25	31	44.28	0.099
Scant material	22	27.5	28	40	-

As is clear from table 2, correlation between NERD and ERD in cytology was not found to be statistically significant ($p > 0.05$).

The cytological spectrum seen in patients of GERD included reactive changes with inflammation (56 patients) and inflammatory smears (12 patients). 32 patients revealed an absolutely normal cytology. 50 patients had scant representative material. In the control group, 39 subjects revealed a normal cytology. 1 subject each had inflammatory smears and reactive changes with inflammation. 9 subjects out of 50 controls had scant representative material.

Presence of reactive changes with inflammation revealed a statistically significant correlation between GERD and controls ($p < 0.05$). However, the presence of inflammatory cells did not reveal a statistical significance. ($p = 0.136$)

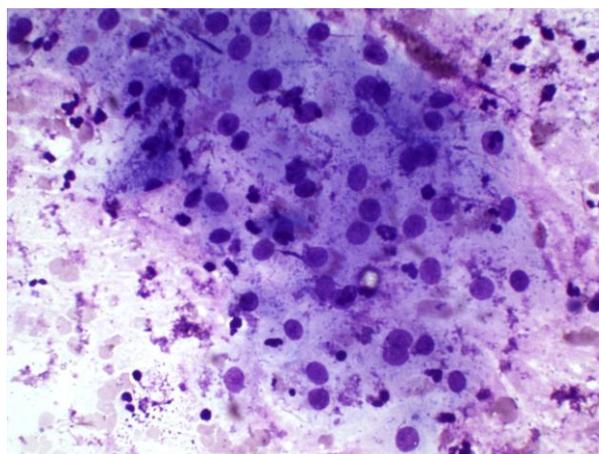


Figure 1: Squamous epithelial cells revealing lymphocytes and neutrophils.

The sensitivity of cytology in our study was 68% and specificity was 95.12%.

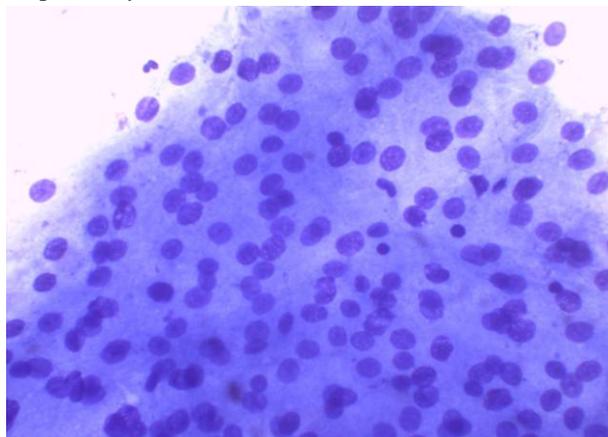


Figure 2: Reactive changes in squamous cells (enlarged nuclei, bi- and multi-nucleation, prominent nucleoli)

The sensitivity of cytology in our study was 68% and specificity was 95.12%.

4. Discussion

We did not come across any studies defining any diagnostic parameters in cytology in GERD patients despite extensive search. However, various authors have suggested that brush cytology of reflux esophagitis has non-specific cytological features chiefly comprising of reactive changes with inflammation and inflammatory cells as was also seen in our study.[3]

Jhala *et al* in Atlas of Diagnostic Pathology have emphasized the importance of “school of fish” appearance in sheets of reactive squamous cells and mixed inflammatory cell infiltrate predominantly composed of neutrophils in cytological samples of GERD cases.[3]

Geisenger *K et al* in Comprehensive cytopathology have suggested that there are no specific cytomorphologic features in GERD. Brushings reflect the spectrum of histologic changes and thus consist of a nonspecific picture of acute inflammation with/without reactive epithelial changes. In our study 1/3rd of the cases of GERD had scant cell material and hence could not be analyzed. Among the remaining 100 cases with representative material on cytology, 56 revealed reactive changes with inflammation. Out of these 56 patients with reactive changes in cytology, 54 revealed papillary elongation and/or basal cell hyperplasia in histopathology. Thus, as mentioned by Geisenger *et al*, we also observed a good correlation between the cytological and histopathological findings. Since the findings are non-specific with ill-defined diagnostic criteria which can accompany a large number of conditions, cytology cannot be used alone as a diagnostic modality in GERD.[4]

Presence of reactive changes with inflammation revealed a statistically significant correlation between GERD and controls ($p < 0.05$). However, the presence of inflammatory cells did not reveal a statistical significance. ($p = 0.136$)

Geisenger *K et al* have emphasized that reactive epithelial cell in cytology correlate with basal cell hyperplasia and papillary elongation on histology. Inflammatory cells on cytology correlate with the presence of intra-epithelial neutrophils on biopsy. In our study we found that there were reactive changes in the sheets of squamous epithelial cells and their presence revealed a statistically significant correlation when compared with controls.[4]

In biopsy, we found papillary elongation and basal cell hyperplasia in a significant number of GERD cases and both these parameters revealed a statistically significant correlation between cases and controls. Thus, as suggested by Geisenger *K et al*[4], we also affirm that basal cell hyperplasia and papillary elongation on biopsy are basically expressed as reactive epithelial cell changes on cytology. However, on comparing reactive changes in cytology and histopathology, we observed that in histopathology, 106 out of 150 cases had basal cell hyperplasia and papillary elongation while only 56 cases out of 150 showed reactive changes in cytology smears. Out of the 56 cases with reactive changes in cytology, 49 had papillary elongation and/or basal cell hyperplasia in histology. We had 50 cases with scant cell material on cytology. Out of these 50 cases, 46 had papillary elongation and/or basal cell hyperplasia. Hence, the discrepancy between cytology and histology is predominantly due to the scant cell material in cytology.

Inflammatory smears in our study were not found to be statistically significant between cases and controls on cytology, while in biopsy there was a statistically significant correlation when presence of intra-epithelial neutrophils was assessed. The probable explanation for the discrepancy is that 33.33% of our GERD cases had scant cell material and hence, were inconclusive on cytology.

The sensitivity of cytology in our study was 68% and specificity was 95.12%.

Hence, we observed that cytology in GERD cases is limited by scant cell yield due to possibly intact mucosal membranes in especially NERD cases. Also, no defined diagnostic criteria are established in cytology for accurate assessment. So, cytology cannot be truly relied upon and can only be used as an adjunct to histopathology with both being complementary to each other as suggested by Geisenger *K et al*. [5]

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