

## ORIGINAL ARTICLE

## Significance of micronuclei (MN) scoring in various epithelial lesions- special emphasis on Breast lesions

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**BACKGROUND AND OBJECTIVES:** Cancer is genomic disease associated with genetic damage accumulation. Majority of solid tumors show large number of chromosomal aberrations. Carcinoma of breast is on rise in our country. Like other cancers even breast carcinomas are known to have chromosomal instabilities that play an important role in cancer development and progression **METHODS:** The study consisted of 100 patients in which breast lesions, cervical lesions and liver lesions were included. Patients of all ages and both sexes were included. Our hospital is a tertiary care hospital and most of the patients are from lower economic group. After staining & mounting procedure micronuclei were counted. Scoring is done per 1000 epithelial cells in light microscopy. **RESULTS:** MN scoring on the cytology smear is a tedious process but it is cheap & readily be done in any laboratory in routinely processed & stained smears **CONCLUSION:** MN scoring on the epithelial cells of cervix could be used as biomarker in cancer screening . This is an easy, simple, reliable, reproducible & objective test which can be performed on routinely stained pap smears.

**Keywords:** Micronucleus, Scoring, Genetic**INTRODUCTION**

Cancer is genomic disease associated with genetic damage accumulation. Majority of solid tumors show large number of chromosomal aberrations.<sup>1</sup> Carcinoma of breast is on rise in our country. Like other cancers even breast carcinomas are known to have chromosomal instabilities that play an important role in cancer development and progression. These instabilities can involve various oncogenes and tumor suppressor genes. Chromosomal instabilities in breast cancer occur in form of p53 mutations, BRCA1 & BRCA2 mutations, CHEK mutations. These occurs in both familial and sporadic carcinomas.

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Though for developing cervical cancer human papilloma virus [HPV0 has important role, like breast carcinoma cervical carcinoma have chromosomal instabilities in form of MDM2 gene mutation, RB gene mutation. p 53 is rarely mutated in cervical carcinoma.<sup>2</sup> Thus screening for chromosomal instabilities is very important. The screening for chromosomal instabilities can be done by using micronuclei scoring. In breast carcinoma patient's occurrence of micronuclei has been investigated in lymphocytes which is procured from peripheral blood.<sup>3-6</sup> It is reported significant increase of micronuclei in buccal smears of patients with carcinoma of breast raising the possibility that genetic damage in these patients is generalized and micronuclei can act as bio monitoring of DNA detection in these cases.<sup>7</sup> The aim and objective of the study was to evaluate significance of micronuclei in various benign and malignant epithelial lesions

and to establish the importance of micronucleus scoring in cytology smear.

**MATERIALS AND METHODS**

The present study was a prospective study of micronuclei scoring of various epithelial lesions special emphasis on breast lesions conducted at department of pathology, M. P. Shah Govt. Medical College, Guru Gobindsingh Government hospital, Jamnagar. Cytological smears and histopathological specimens received in respective cytopathology and histopathology section of the pathology department over a period of two years (November 2016 to November 2018) were included in the study. The study consisted of 100 patients in which breast lesions, cervical lesions and liver lesions were included. Patients of all ages and both sexes were included. Our hospital is a tertiary care hospital and most of the patients are from lower economic group. Patient's age, clinical presentation, detailed clinical history, radiological findings and other investigations were noted.

**Cytological Examination of Breast Lesions**

After clinical evaluation of patients ,consent of patient is taken. Then FNAC is taken. Aspirated material is put on glass slides. Smears are fixed in 95% alcohol and stained with Pap or H & E stain. & MGG stain.

**Cytological Examination of Cervical Smears**

Prepared slides of cervical smear are received from gynecology department. The smears are fixed with 95% alcohol. These smears were stained with Pap stain. After staining & mounting procedure micronuclei were counted. Scoring is done per 1000 epithelial cells in light microscopy.

**Scoring Criteria**

- Intact cytoplasm and relatively flat cell position on the slide
- Little or no overlap with adjacent cells
- Little or no debris

- Nucleus normal and intact, nuclear perimeter smooth and distinct
- Texture of micronucleus similar to that of nucleus
- Staining intensity similar to that of nucleus
- It should be as same focal plane as nucleus

**RESULT AND DISCUSSION**

Out of 100 cases 70 cases were of breast lesions which includes various benign breast lesions like, acute mastitis, granulomatous mastitis, fibroadenoma, fibroadenosis, fibrocystic diseases, phylloides tumor and epithelial hyperplasia with atypia, suspicious for carcinoma & malignant lesions of breast. 16 cases were of cervical smear in which HSIL or SCC were diagnosed.14 cases were of liver in which metastasis were diagnosed

**Table No. 1 Site wise distribution of cases (n=100)**

Site of collection	No. of cases
Breast	70
Cervix	16
Liver	14
Total	100

**Table 2: distribution of breast lesions according to age( n=70)**

Age (years)	Benign	Malignant	Total no. Cases
10 – 25	09 (12.86%)	01(1.42%)	10
26 – 50	21 (30%)	20(28.57%)	41
51 – 75	02 (2.86%)	17(24.28%)	19
TOTAL	32	38	70

**Table 3: Distribution of breast lesions on basis of nature of disease on cytological smears(n=70)**

Nature of disease	No. Of cases	Percentage
Benign Breast lesions	32	45.71%
Ductal hyperplasia with atypia	3	4.28%
Suspicious for carcinoma	6	8.57%
Malignant breast lesions	29	41.42%
TOTAL	70	

**Table 4: Nature wise distribution of cervical cases(n=16)**

Nature of disease	No. Caes	Percentage
HSIL	15	93.75%
SCC	1	6.25%
TOTAL	16	

**Table 5: Gender wise distribution of liver cases(n=14)**

Sex	No. Of cases	Percentage
Female	10	71.42%
Male	4	28.57%
TOTAL	14	

**Table 6: Nature wise distribution of liver cases(n=14)**

Nature of disease	No. Of cases	Percentage
Metastasis from ductal carcinoma of breast	6	42.85%
Metastasis from squamous cell carcinoma	5	35.72%
Metastasis from in liver	3	21.43%
TOTAL	14	

**Table 7: Occurance Of MN In Various Lesions On Cytological Smears(N=33)**

Lesion	No. Of cases	Percentage
Fibroadenosis with epithelial hyperplasia	1	3.03%
Ductal hyperplasia with atypia	3	9.09%
Suspicious for carcinoma of breast	2	6.06%
Carcinoma of breast	17	51.52%
Metastasis from ductal carcinoma	3	9.09%
Metastasis from SCC	1	3.03%
SCC	1	3.03%
HSIL	5	15.15%
TOTAL	33	

**Table 8: MN Scoring in Breast Lesions (n=70)**

No. Of mn/1000 cells	No. Of cases	Percentage
0	47	67.14%
1	13	18.57%
2	07	10.00%
3	03	4.29%
TOTAL	70	

**Table 9: comparison of MN Scoring in benign versus malignant breast lesions(n=70)**

MN	No. Of malignant breast lesions	No. Of benign breast lesions	Total no. Of cases
PRESENT	22(31.43%)	01(1.43%)	23
ABSENT	16(22.86%)	31(44.28%)	47
TOTAL	38	32	70

**Table 10 : Mean Micronuclei Scoring In Breast Lesions(N=70)**

Nature of disease	No. Of cases	Mean MN scoring
Benign lesions	32	0.031±0.177
Malignant lesions	38	0.92±0.96
TOTAL	70	

Out of 70 cases 32 cases were benign & 38 cases were malignant. For benign diseases Mean MN score is 0.031±0.177 whereas for malignant diseases Mean MN score is 0.92±0.96. Two tailed probability is <0.0005.

**Table 11: MN Scoring In Cervical Lesions (N=16)**

No. Of mn /1000 cells	No. Of cases	Percentage
0	10	62.5%
1	6	37.5%
TOTAL	16	

**Table 12: MN Scoring In Liver Lesions (N=14)**

No. Of mn/1000 cells	No. Of cases	Percentage
0	10	71.43%
1	3	21.43%
2	1	7.14%
TOTAL	14	

Samanta et al had done study on total 71 cases of breast lesions in which 31 cases of fibroadenoma & 40 cases of IDC were included in year 2010.<sup>3</sup> A. Hemalatha et al had done study on total 80 cases in which 40 cases of fibroadenoma & 40 cases of IDC were included.<sup>4</sup> In present study out of 100 cases 70 cases of breast lesions are included, in which 32 cases are of benign lesions & 38 cases are of IDC. Only few studies have described the occurrence of micronucleus in breast carcinoma in fine needle aspiration cytology. Samanta S et al. have reported role of micronucleus scoring in fine needle aspirates in ductal carcinoma of breast.<sup>3</sup> They have concluded that micronuclei scoring is significantly higher in cases of invasive ductal carcinoma (IDC) than fibroadenoma. A. Hemalatha et al have also done MN scoring in breast aspirates, they have also reported significantly higher score in IDC than in fibroadenoma.<sup>4</sup> In present study we noticed a significant difference in occurrence of micronuclei

between benign and malignant cases of breast lesions. Similar findings has been described by Samanta S and A. Hemalatha et al<sup>3,4</sup>

**Table 13: Comparison Of MN Scoring In Breast Lesions With Previous Study**

Study	Total no. Cases	Mean mn score in benign breast lesions	Mean mn score in malignant breast lesions
Samanta et al (2010) <sup>3</sup>	71	0.6 ±1.1	13.6±12.8
A. Hemalatha et al (2014) <sup>4</sup>	80	1.8 ±1.9	12.1±9.2
Present study (2017)	70	0.03 ±0.17	0.92±0.97

They have concluded significantly higher MN scoring occur in neoplastic condition than benign.<sup>1</sup> Similar study done by Gayathri et al<sup>5</sup> and conclusion was same as Samantha's study. Guzman et al<sup>10</sup> had done study relieving positive correlation between micronuclei frequency & dysplasia in papnicolau stain.

**Table14: Comparison Of MN Score In Cervical Lesions(HSIL)**

Study	No. Of cases	Mean mn scoring
Samanta et al (2011) <sup>1</sup>	30	21.30±17.18
Gayathri et al (2012) <sup>5</sup>	31	8.03±1.64
Present study	15	0.37±0.50

In present study only cases of HSIL were included, in 15 cases of HSIL mean MN scoring is 0.37±0.50. It is less than that of previous two studies. In present study 14 cases of metastasis to liver from epithelial origin are taken. In which mean micronuclei scoring is 0.357±0.63.

## CONCLUSION

MN formation is generally considered as manifestation of genetic damage or chromosomal breakage. However, many conditions like radiation, drugs, pollutants, even normal aging process may be responsible for MN formation. So, increased MN is suggestive but not diagnostic of pre neoplastic conditions and caution should be exercised in the form of meticulous clinical history & examination. MN scoring on the cytology smear is a tedious process but it is cheap & readily be

done in any laboratory in routinely processed & stained smears. MN scoring on the epithelial cells of cervix could be used as biomarker in cancer screening. This is an easy, simple, reliable, reproducible & objective test which can be performed on routinely stained pap smears.

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