



Original Research Article

Evaluation of p53 in breast cancer and its correlation with various histological prognostic factors

Kriti Arora^{1,*}, Ruchee Khandelwal¹, Hema Pant¹

¹Dept. of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India



ARTICLE INFO

Article history:

Received 13-03-2020

Accepted 16-04-2020

Available online 19-08-2020

Keywords:

Breast cancer

ER

PR

Her-2neu

P53

ABSTRACT

Background: Carcinoma of the breast is the most common non-skin malignancy in women. The p53 gene is one of the most commonly mutated genes described in human neoplasia. Mutant p53 protein has greater stability and longer half time than the wild type protein that can be detected by Immunohistochemistry. This study was conducted to evaluate the expression of p53 in breast carcinoma and its correlation with various histological prognostic markers to determine its significance as a prognostic marker in breast cancer.

Materials and Methods: The prospective study included 52 modified radical mastectomy specimens diagnosed as breast cancer in the Department of Pathology at SRMSIMS, Bareilly between November 2016 and April 2018. Routine H&E staining and immunohistochemical analysis for ER, PR, Her2/neu and P53 was carried out in all the cases.

Results: Majority of the cases belonged to the age group 30-39 years and the most common cancer type was infiltrating ductal carcinoma. Significant correlation of p53 was observed with ER and PR expression, however no significant correlation could be found with tumor type, grade, size, type of margin, necrosis, stromal response, lymphovascular invasion, lymph node status and Her2/neu status.

Conclusion: P53 was found to have a significant inverse correlation with ER and PR expression only. The results do not resolve whether detectable p53 protein expression represents a random product of dedifferentiation or an important feature of the malignant phenotype, playing a key role in tumor behavior.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (<https://creativecommons.org/licenses/by-nc/4.0/>)

1. Introduction

Carcinoma of the breast is the most common non-skin malignancy in women and is second only to lung cancer as a cause of cancer death. A woman who lives to age of 90 has one in eight chance of developing breast cancer.¹

The location of breast carcinoma is usually indicated in relation to the breast quadrants. Approximately 50% are in upper outer quadrant. Majority of the breast malignancies are adenocarcinoma other types are less than 5%.² The major risk factors for the development of breast cancer are Age, Age at menarche, Age at first live birth, First – degree relatives with breast cancer, Atypical hyperplasia, Race/Ethnicity, Estrogen exposure, Breast density, radiation exposure, Carcinoma of the contralateral

breast or endometrium, geographic influence, diet, obesity, environmental toxins and tobacco while exercise and breast feeding decrease the risk of breast cancer.³

The outcome for women with breast cancer varies widely and is related to various prognostic factors. Major prognostic factors are age, BRCA1 status, early diagnosis, presence and absence of invasiveness, tumor size, tumor type, microscopic grade, type of margin, tumor necrosis, stromal reaction, microvessel density, nipple invasion, ER and PR receptors, Her2/neu status and axillary lymph node metastasis.²

In past two decades, the treatment of breast cancer has undergone dramatic change and a much wider range of therapeutic options are now available. As the range of options for the treatment widens, it becomes increasingly important that the clinician is provided with accurate prognostic information on which to base the therapeutic

* Corresponding author.

E-mail address: kritiarora.rka@gmail.com (K. Arora).

decision. A wide range of potential prognostic factors have now been studied, some well established, eg. ER/PR, HER2/neu expression while some at the developmental stage eg. p53, bcl2, Ki-67, Cyclin D1, Cyclin E, ER β , etc.⁴

Nearly one third of breast cancers have mutation in p53, a tumor suppressor gene. Literature suggests that over-expression of HER-2 and p53 may have an adverse effect in breast cancer.⁵

The p53 gene is one of the most commonly mutated genes thus far described in human neoplasia with mutations estimated to occur in upto 50% of all cancers.⁶ First described in 1979, and initially believed to be an oncogene, p53 was the first tumor suppressor gene to be identified.⁷ It is located on short (p) arm of chromosome 17 and is another proved breast cancer progression gene that regulates cell cycle and DNA repair. Unlike normal p53, nonfunctional mutated p53 accumulates in the nucleus of tumor cells, and therefore, it can be detected by immunohistochemical analysis.⁸

The association between p53 alterations and clinical outcome in breast cancer has been the subject of numerous investigations. P53 immunoreactivity could bear some prognostic significance.⁹ Therefore this study was conducted to evaluate the expression of p53 in breast carcinoma and its correlation with various histological prognostic markers to determine its significance as a prognostic marker in breast cancer.

2. Material and Methods

The present study was conducted in the Department of Pathology in our institute. Study duration was from November 2016 to April 2018. A total of 52 cases presenting with breast lumps in surgical OPD and diagnosed as suffering from breast cancer on FNAC/Trucut needle biopsy and who further underwent modified radical mastectomy in the department of surgery were enrolled for the study. The mastectomy specimens received in the Department of Pathology were examined for gross details. Representative sections were taken and processed in a tissue processor to make paraffin embedded blocks. 3 to 5 μ m thick sections were cut and stained with Haematoxylin and Eosin (H & E) and tumor sections were also stained with ER, PR, Her2/neu and p53 antibodies (IHC). The stained sections were studied in detail for the presence of tumor, type of tumor (WHO classification 2012) and grade of tumor (Nottingham's grading system), type of tumor margin, presence and absence of necrosis, lymphovascular invasion, stromal reaction and lymph node status.

P53 scoring was done as per semi quantitative method as described by Wee et al¹⁰ which takes into account the intensity of staining and the percentage of nuclei stained. Total score was then obtained by the sum of intensity score and percentage score, ranging from 0-6 (Table 1).

Table 1:

Intensity score	
No stain	0
Weak stain	1
Intermediate stain	2
Strong stain	3
Percentage score	
<10%	1
10%-50%	2
>50%	3

2.1. Scoring system for ER and PR4

Scoring for ER/PR was done using the Allred score which takes into account proportion and intensity of positive tumors cells which are scored from 0-5 and 0-3 respectively. Total score is obtained by the sum of proportion score and intensity score, ranging from 0-8 (Table 2).

Table 2:

Score for proportion
0 = No staining
1 = <1% Nuclei staining
2 = 1%-10% Nuclei staining
3 = 11%-33% Nuclei staining
4 = 34%-66% Nuclei staining
5 = 67%-100% Nuclei staining
Score for intensity
0 = No staining
1 = Weak staining
2 = Moderate staining
3 = Strong staining
A score >2 has been adjudged the minimum score for defining ER and PR positive breast cancer

2.2. Scoring system for HER2/neu4

The scoring method recommended is a semiquantitative system based on the intensity of reaction product and percentage of membrane positive cells, giving a score range of 0 to 3+ (Table 3).

Association/correlation of p53 expression with independent variables such as histological type, grades of tumor, tumor size, tumor margin, necrosis, lymphovascular invasion, stromal reaction, lymph node status, ER, PR, and Her2/neu expression was analysed by applying Pearson's Chi Square test, Fisher's exact test. Statistical analysis was performed using SPSS version 23 and p-value of less than 0.05 was considered statistically significant at 95% level of significance.

3. Result

A prospective study was undertaken on 52 mastectomy specimens diagnosed as breast cancer in the Department

Table 3:

Score to Report	HER-2 Overexpression Assessment	Protein Staining Pattern
0	Negative	No staining is observed, or membrane staining in fewer than 10% of tumor cells
1+	Negative	A faint or barely perceptible membrane staining is detected in more than 10% of tumor cells. The cells are only stained in part of the membrane.
2+	Borderline	A weak to moderate complete membrane staining is observed in more than 30% of tumor cells.
3+	Positive	A strong complete membrane staining is observed in more than 30% of the tumor cells.

of pathology between November 2016 and April 2018 at SRMS IMS, Bareilly. The tumor was typed, graded and evaluated for different histopathological prognostic parameters like tumor size, type of margins, lymphovascular invasion, necrosis, lymph node status and stromal reaction. Scoring for ER, PR, Her2/neu and p53 was also done on tumor sections. Any possible correlation between P53 expression and tumor type, tumor grade, tumor size, type of tumor margin, stromal reaction, presence and absence of necrosis, lymphovascular invasion, lymph node status, ER, PR and Her2/neu status was tried to be determined.

The age of the patients in the present study ranged from 25-76 years. Mean age of presentation was 43.1 years. Majority of the cases, 17 (32.7%) belonged to the age group, 30-39 years followed by 14 (26.9%) cases in the age group 40-49 years. Male to Female ratio was 51:1. The most common type of tumor was found to be infiltrating ductal carcinoma constituting 43 (84.6%) cases, followed by 6 (9.6%) cases of medullary carcinoma, 2 (3.8%) cases of infiltrating ductal carcinoma with medullary features and 1 (1.9%) case of lobular carcinoma. Most of the cases of infiltrating ductal carcinoma belonged to age group of 30-39 years. Medullary carcinoma was found to be most common in the age group 40-49 years. Nottingham histological grade 2 was the most common grade in the present study comprising 30 (57%) cases followed by grade 3 with 13 (25%) cases and grade 1 with 9 (18%) cases. In the present study the tumor size was classified according to the TNM classification. In 31 (59.6%) cases the tumor size was between 2-5 cm followed by 19 (34.6%) cases of tumor size > 5 cm and 2 (5.85%) cases of tumor size <2 cm. In the present study 38 (75%) cases had infiltrative type of tumor margins while only 14 (25%) cases had pushing type of tumor margins. Tumor necrosis is a less

commonly studied prognostic factor. In this study necrosis was present in only 23 (44%) cases. Inflammatory stromal response was found in 29 (56%) cases while 23 (44%) cases either showed only desmoplasia or did not have any stromal response. Lymphovascular invasion which was present only in 22 (42.3%) cases. In the present study 22 (42.3%) cases had 4 or more lymph nodes positive for tumor metastasis, followed by 17 (32.7%) cases which had <4 lymph nodes positive and 13 (25%) cases with no lymph node metastasis. Only 12 (23.1%) cases were positive and 40, (76.9%) were negative for estrogen receptors. Only 19 (36.5%) cases were positive and 33 (63.5%) cases were negative for progesterone receptors. 23 (44%) cases were positive and 29 (56%) cases were negative for Her2/neu expression. 32 (61.5%) cases were positive for p53 expression and only 20 (38.5%) cases were negative.

25 out of 43 cases of infiltrating ductal carcinoma were positive for p53, both the cases of infiltrating ductal carcinoma with medullary features were positive for p53. Of the 6 cases of medullary carcinoma 4 were positive for p53. Only one case of lobular carcinoma was included in the study which was negative for p53. No significant association was seen between p53 and tumor type (p value = 0.52). 5 (9.6%) cases of grade 1, 19 (36.5%) cases of grade 2 and 8 (15.4%) cases of grade 3 were positive for p53 expression. No significant correlation was seen between the tumor grade and p53 expression (p value = 0.9). 1 (1.9%) case of tumor size < 2 cm, 17 (32.7%) cases of tumor size between 2-5 cm and 14 (26.9%) cases of tumor size \geq 5 cm were positive for p53 expression. No significant correlation was seen between tumor size and p53 expression. Majority of tumors in this study had infiltrative type of tumor margin and 25 (48.1%) cases with infiltrative type of tumor margin were positive for p53. No significant association was found between type of margin and p53 expression. No significant correlation of p53 expression was observed with necrosis, stromal response, lymphovascular invasion. 14 (26.9%) cases with \geq 4 lymph nodes were positive for p53 expression followed by 11 (21.1%) cases with 1-3 lymph nodes and 7 (13.5%) cases with no positive lymph nodes. No significant correlation was found between lymph node status and p53 expression (p value = 0.8). In our study 28 (53.8%) ER negative cases were positive for p53 expression and significant inverse correlation was seen between ER and P53 expression (p value = 0.02). 24 (46.2%) PR negative cases were positive for p53 and a significant inverse correlation was seen between PR and p53 expression. P53 expression was positive in 14 (26.9%) Her2/neu positive cases and 18 (34.6%) Her2/neu negative cases. No significant correlation was found between Her2/neu and p53 expression.

4. Discussion

Breast cancer is no longer seen as a single disease but rather a multifaceted disease comprising of distinct biological

subtypes with diverse natural history, presenting a varied spectrum of clinical, pathologic and molecular features with different prognostic and therapeutic implications.¹¹

Pathological variables such as tumor size, histological type, histological grade, lymph node metastasis, vascular space invasion, tumor cell proliferation, extent of ductal carcinoma in situ are the predictors of prognosis and for the need of adjuvant therapy. Biomarkers such as ER, PR and HER-2neu expression represent the most acceptable ones for predicting prognosis, response/resistance to treatment and in deciding the use of newer drugs such as trastuzumab in the case of HER-2over expression.⁸

Mutations in the p53 gene or increased expression of the p53 protein as an indirect marker of a mutation have been described as prognostic factors for a long list of human malignant tumours, including breast cancer. Recent studies have suggested that p53 status might have a different predictive value for the efficacy of anthracycline/alkylating agent based chemotherapy regimen between triple negative & non triple negative breast cancers.¹²

In the present study age of the patients ranged from 25 to 76 years and maximum number of cases were between 30-39 years (32.7%) followed by 40-49 years (26.9%). The mean age of presentation was 45.31 ± 10.81 years. The findings are almost similar to that reported by Sheikhpour et al (44.75 ± 9.5 years)¹³ and Kanna et al (58% cases between 36 to 50 years of age),¹⁴ while the patients were slightly younger than cases reported by Patnayak et.al (50.7 ± 11.5 years),⁵ Abdollahi et.al (50.2 ± 12.3 years)¹⁵ and Gupta et.al (50 years).⁸ It is a documented fact that advancement of age increases the risk of breast cancer and most women are over the age of 60 years when diagnosed.¹³ Although there is evidence that Indian women are more likely to develop breast cancer at earlier ages than their Western counterparts.¹⁶

In this study 84.6% cases were of infiltrating ductal carcinoma which was in concordance with the findings of Sheikhpour et.al (84.6% cases),¹³ Goel et.al (85% cases),¹⁷ Patnayak et.al⁵ and Gupta et.al (86.1% cases)⁸. Other subtypes included in the study were infiltrating ductal carcinoma with medullary features, medullary carcinoma and lobular carcinoma.

57% cases of breast carcinomas in this study belonged to grade 2 followed by 25% cases of grade 3. Similar observations were made by Shoukhouh et al (54.8%),¹⁸ Gupta et al.(45.8%),⁸ Patnayak et al (60.9%)⁵ cases and Abdollahi et al. observed 82.7% cases of grade 2.¹⁵ Frequency of grade 1 cases is variable in different studies. However Piplani et al.,¹⁹ Neharika et al.²⁰ and Goel et al.¹⁷ reported a higher frequency of grade 3 tumors.

One of the most important and well established prognostic factor in carcinoma breast is tumor size.³ In this study tumor size was divided into three categories as per the TNM classification system. 31(59.6%) cases had tumor size

between 2-5 cm constituting the largest group. 19 (36.5%) cases had tumor size >5 cm. This is in concurrence with the results obtained by Patnayak et al,⁵ Piplani et al,¹⁹ Gupta et al⁸ and Neharika et al²⁰ who found 79.6%, 67.7%, 63.9%, 53.9% cases of tumor size between 2-5 cm in their studies respectively, whereas in the study done by Taucher et al the tumors were predominantly less than 2 cm in size which could be due to more awareness and early detection programs prevalent in the western countries.²¹

Type of tumor margin, presence and absence of necrosis, inflammatory type of stromal response and lymphovascular invasion are described as factors associated with poor prognosis in the literature,⁴ but these are less frequently studied. 23 (44%) cases had necrosis associated with the tumor. Carter and colleagues gave a figure of 40%, compared with 60% estimated by Fisher and coworkers.⁴

22 (42.3%) cases showed lymphovascular invasion. The reported range for lymphovascular invasion extends from 10% to 54%.⁴

In this study 22 (42.3%) cases had ≥ 4 lymph nodes positive for tumor deposits, followed by 17(32.7%) cases having 1-3 lymph nodes positive and 13(25%) cases with no lymph positive for tumor deposits. Similar observations were made by Goel et al.¹⁷ and Neharika et al.²⁰ Friedrichs et al. observed that risk of recurrence increases with the number of lymph nodes involved.²²

The prevalence of hormone receptor positive breast cancer in Asian countries has been found to be lower than those in the western world.²³ Indian literature reports estrogen receptor positivity varying between 30-50%.²⁴ In the present study we found only 12 (23.1%) cases positive for estrogen receptors. Desai et al.,²⁵ Abdollahi et al.,¹⁵ Neharika et al.,²⁰ Piplani et al.¹⁹ and Patnayak et al.⁵ reported prevalence of 32.6%, 36.4%, 38.16%, 41.5% and 47.6% ER positive cases respectively.

Progesterone receptors were found to be positive in slightly more number of cases as compared to ER, constituting 19 (36.5%) cases positive and 33 (63.5%) cases with negative expression. Dutta et al.,²⁶ Desai et al.,²⁵ Mudduwa et al.,²⁷ Patnayak et al.,⁵ Ambroise et al.²⁸ and Adollahi et al⁵ reported 30%, 46.1%, 48.3%, 48.8%, 51% and 58.9% PR positive expression respectively.

In this study we found 23 (44%) cases positive for Her2/neu expression. Considerable variation is reported in frequency of Her2/neu positivity. James et al.²⁹ Patnayak et al,⁵ Vadiyanathan et al.³⁰ and Neharika et al²⁰ reported 29%, 29.6%, 43.2% and 51.32% positivity respectively.

In the present study 32 (61.5%) cases were positive for p53 expression. This was quiet close to observations of Patnayak et al,⁵ Song et al³¹ and Sekar et al³² who reported 69.2%, 51.6% and 71.6% p53 positive expression respectively. Many authors have reported low positivity of 22%,¹⁴ 28.8%,¹³ 29.6%,³³ 34%,³⁴ 36%,³⁵ 37.1%,⁵ 37.4%,¹⁵ 38.5%,²² 45.5%,³⁶ 45.7%,¹⁷ 47.4%²⁰

and 48.9%.²³ In contrast to this Gupta et al⁸ reported 88.9% p53 positive expression. This variability in the results may be attributed to the diversity of procedures and reagents used by different investigators. Significant differences have been reported³⁶ in p53 immunoreactivity depending upon the antibody used. Another important difference among the reported studies was the lack of a standardized immunohistochemical criteria to classify a carcinoma as p53 positive.

In our study we did not observe any significant association between p53 expression and type of tumor. This is in concordance with Sheikhpour et al¹³ and Goel et al.¹⁷ In contrast to this Jacquemier et al³⁷ observed a significant correlation. This could be because we did not have significant number of different subtypes of breast carcinoma unlike their study.

In our study the p53 expression in grade 1, 2 and 3 tumors was found to be 55.6%, 63.3% and 61.5% respectively, unlike the study done by Ranade et al³⁸ in which the expression of p53 increased with the tumor grade and was 33%, 52% and 67% respectively in grade 1, 2 and 3. This study showed no significant association between grade of tumor and p53 expression. This is in accordance with Sheikhpour et al¹³ and Abdollahi et al.¹⁵ However in contrast to our study many studies have reported a significant positive association (Cattoretti et al,³⁶ Thor et al,³⁹ Rosen et al,⁴⁰ Friedrichs et al, Jacquemier et al,³⁷ Neharika et al,²⁰ Shoukhouh et al,¹⁸ Piplani et al,¹⁹ Al-Joudi et al,³³ Sekar et al,³² Kanna et al,¹⁴ Goel et al.¹⁷ and Gupta et al).⁸ This variation could be because of low sample size in our study.

In this study a higher frequency of cases with tumor size ≥ 5 cm showed p53 positive expression as compared to the number of cases with tumor size between 2-5 cm but as the majority of the cases in our study had tumor size between 2-5 cm therefore higher overall p53 positivity was observed in this group i.e in 17 (32.7%) cases. No significant correlation was observed between tumor size and p53 expression. Our findings are similar to the findings of Friedrichs et al,²² Shoukhouh et al,¹⁸ Al-Joudi et al,³³ Abdollahi et al,¹⁷ Goel et al¹⁷ and Gupta et al.⁸ However Neharika et al²⁰ found a significant correlation between the size of tumor and p53 positive expression.

48.1% cases with infiltrative tumor margin and 11.5% cases with pushing margins were positive for p53 expression and no significant correlation was seen between p53 expression and type of tumor margin. We could not find similar correlation being done by any other study.

Similarly no correlation was seen between p53 expression and presence and absence of necrosis whereas Kanna et al.¹⁴ reported that cases with p53 positivity demonstrated mild necrosis in the tumors.

29 (56%) cases in this study had lymphocytic stromal response and 20 of these 29 cases were positive for p53

expression. However, no significant correlation was seen between p53 expression and lymphocytic type of stromal reaction. Kanna et al.¹⁴ reported p53 overexpression in tumors with severe lymphocytic reaction.

38.5% cases with lymphovascular invasion were positive for p53 expression but no significant correlation was seen between lymphovascular invasion and p53 expression.

No significant correlation was seen between lymph node status and p53 positivity (p value = 0.8) which is in concordance with Jeong Han et al. (p > 0.5),⁴¹ Banulebe et al (p > 0.5),⁴² Friedrichs et al,²² Jacquemier et al,³⁷ Shoukhouh et al,¹⁸ Piplani et al,¹⁹ Goel et al¹⁷ and Al-Joudi et al³³ Kanna et al.¹⁴ found an equivocal p53 status in both positive and negative cases of lymph node metastasis. In contrast to our study Gupta et al. (p = 0.0002),⁸ Ivkovic et al. (p < 0.05),⁴³ Abdollahi et al¹⁵ and Neharika et al.²⁰ found a significant correlation between lymph node status and p53 positivity.

In this study no significant correlation of p53 expression was observed with type of tumor, tumor grade, tumor size, type of tumor margin, presence and absence of necrosis, lymphocytic stromal reaction and lymphovascular invasion. Hence p53 does not seem to be associated with tumor aggressiveness.

Estrogen receptors were negative in 40 cases and of these 28 cases were positive for p53 expression. A significant correlation was found between ER and p53 expression. We observed that p53 is inversely associated with ER. Our results are in concordance with Cattoretti et al,³⁶ Thor et al,³⁹ Rosen et al,⁴⁰ Friedrichs et al,²² Jacquemier et al,³⁷ Neharika et al,²⁰ Shoukhouh et al,¹⁸ S Han Jeon et al⁴¹ and Ranade et al.³⁸ However Piplani et al¹⁹ and Al-Joudi et al³³ failed to find any significant correlation.

A statistically significant negative correlation was also found between PR and p53 expression which is in concordance with the studies done by Friedrichs et al,²² Jacquemier et al.,³⁷ Neharika et al²⁰ Shoukhouh et al⁸ and Ranade et al.³⁸ However, Piplani et al¹⁹ and Al-Joudi et al³³ did not find any significant association between the two.

However, no significant correlation was seen between Her2/neu and p53 expression, which is similar to Abdollahi et al¹⁵ and S Han Jeong et al.⁴¹ In contrast Patnayak et al,⁵ Rashed et al.,³⁴ L Ding et al⁴⁴ and Neharika et al²⁰ reported a significant positive association between Her2/neu expression and p53 expression. Coexistence of Her2/neu overexpression and p53 protein accumulation has been suggested to be a strong prognostic molecular marker in breast cancer.⁴⁵

The results of this study do not resolve whether detectable p53 protein expression represents a random product of dedifferentiation or plays any significant role in tumor behavior.

5. Conclusion

In present study highest incidence of infiltrating ductal carcinomas was noted in age group 30 - 39 years and of medullary carcinomas in 40–49 years. No statistically significant association was observed between p53 expression and type of tumor, grade of tumor, size of tumor, lymphovascular invasion, necrosis, stromal reaction, lymph node status and Her2/neu expression. Thus p53 does not seem to be related to tumor aggressiveness. The only significant correlation was observed with ER and PR expression. P53 was found to be inversely correlated with ER and PR. The results do not resolve whether detectable p53 protein expression represents a random product of dedifferentiation or an important feature of the malignant phenotype, playing a key role in tumor behavior. Although no significant correlation was seen between p53 expression and type of tumor, grade of tumor, size of tumor, lymphovascular invasion, necrosis, stromal reaction, LN status and Her2/neu expression, p53 expression increased with tumor size, infiltrative tumor margins, presence of necrosis, lymphocytic stromal response and lymphovascular invasion. Thus, the present study cannot definitely comment on their probability of association due to small individual sample size; and therefore this necessitates follow-up studies with a larger sample size.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

- Lester SC. The breast. In: Kumar V, Abbas AK, Aster JC, editors. Pathologic basis of disease. Elsevier; 2014. p. 1043–71.
- Breast JR. Rosai and Ackerman's Surgical Pathology. 10th ed. and others, editor. Elsevier; 2012.
- Lester SC. The breast. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. Pathologic basis of disease. Elsevier; 2010. p. 1066–90.
- Ellis IO, Pinder SE, Lee AHS. Tumors of breast. Fletcher CDM, Diagnostic histopathology of tumors. 3rd ed. Churchill: Elsevier:Churchill Livingstone; 2007.
- Patnayak R, Jena A, Rukmangadha N, Chowhan A, Sambasivaiah K, Phaneendra B, et al. Hormone receptor status (estrogen receptor, progesterone receptor), human epidermal growth factor-2 and p53 in South Indian breast cancer patients: A tertiary care center experience. *Indian J Med Paediatr Oncol*. 2015;36(2):117–22.
- Gasco M, Yulug IG, Crook T. TP53 mutations in familial breast cancer: Functional aspects. *Hum Mutation*. 2003;21(3):301–6.
- Gasco M, Shami S, Crook T. The p53 pathway in breast cancer. *Breast Cancer Res*. 2002;4:70–6.
- Gupta KK, Dash AK, Mishra DP. Correlation of p53 expression with clinicopathological characteristics of breast carcinoma. *Ann Pathol Lab Med*. 2016;03:162–70.
- Mazars R, Spinardi L, Bencheikh M, Simony-Lafontaine J, Jeanteur P, Theillet C. p53 mutations occur in aggressive breast cancer. *Cancer Res*. 1992;52:3918–23.
- Wee A, Teh M, Raju GC. Clinical importance of p53 protein in gall bladder carcinoma and its precursor lesions. *J Clin Pathol*. 1994;47(5):453–6.
- Onitilo AA, Engel JM, Greenlee RT, Mukesh BN. Breast Cancer Subtypes Based on ER/PR and Her2 Expression: Comparison of Clinicopathologic Features and Survival. *Clin Med Res*. 2009;7(1-2):4–13.
- Axelrod DE, Shah K, Yang Q, Haffty BG. Prognosis for Survival of Young Women with Breast Cancer by Quantitative p53 Immunohistochemistry. *Cancer Clin Oncol*. 2012;1(1):52–65.
- Sheikhpour R. Immunohistochemical Assessment of p53 Protein and its Correlation with Clinicopathological Characteristics in Breast Cancer Patients. *Indian J Sci Technol*. 2014;7(4):427–79.
- Radha RKN, Viswanathan P, Krishnaswamy B. Histopathology and prognostic indices of carcinoma breast with special reference to p53 marker. *J Clin Diagn Res*. 2014;8(7):4–08.
- Abdollahi A, Sheikhabaei S, Safinejad S, Jahanzad I. Correlation of ER,PR, HER-2 and p53 immunoreactions with clinic-pathological features in breast cancer. *Iranian J Pathol*. 2013;8(3):147–52.
- Costa JM, Tadrou T, Hitton G, Birdsong G. Breast fine needle aspiration cytology utility as a screening tool for clinically palpable lesion. *Acta Cytol*. 1993;37(4):461–77.
- Goel MM, Goel R, Mehrotra A, Nath P, Agarwal PK, Singh K. Immunohistochemical localization and correlation of p53 and PCNA expression in breast carcinoma. *Indian J Exp Biol*. 2000;38:225–30.
- Shokouh TZ, Ezatollah A, Barand P. Interrelationships Between Ki67, HER2/neu, p53, ER, and PR Status and Their Associations With Tumor Grade and Lymph Node Involvement in Breast Carcinoma Subtypes. *Med*. 2015;94(32):e1359.
- Piplani S, Madaan M, Manjari M, Manan R. p53 as a Prognostic Marker in Carcinoma Breast in Correlation with Conventional Estrogen and Progesterone Hormone Receptors. *Annals of Pathology and Laboratory Medicine*. 2016;03(06).
- Neharika, Kumar M, Kumar D, Karki MSP, Khanna K, S. Correlation of p53 Protein Accumulation and HER2/neu over expression with Clinicopathological Characteristics in Carcinoma Breast in Indian Population. *Med Sci*. 2014;13(50):43–51.
- Taucher S, Rudas M, Mader RM, Gnant M, Dubsy P, Bachleitner T, et al. Do we need HER-2/neu testing for all patients with primary breast carcinoma? *Cancer*. 2003;98(12):2547–53.
- Friedrichs K, Gluba S, Eidtmann H, Jonat W. Overexpression of p53 and Prognosis in Breast Cancer. *Cancer*. 1993;72(12):3641–7.
- Ahmed HG, Al-Adhraei MA, Al-Thobhani AK. Correlations of Hormone Receptors (ER and PR), Her2/neu and p53 Expression in Breast Ductal Carcinoma Among Yemeni Women. *Cancer Immunol J*. 2011;4(1):1–9.
- Fisher ER, Redmond CK, Liu H, Rockette H, and BF. Correlation of estrogen receptor and pathologic characteristics of invasive breast cancer. *Cancer*. 1980;45(2):349–53.
- Desai SB, Moonim MT, Gill AK, Punia RS, Naresh KN, Chinoy RF. Hormone receptor status of breast cancer in India: a study of 798 tumours. *Breast*. 2000;9(5):267–70.
- Dutta V, Chopra GS, Sahai K, Nema SK. Hormone Receptors, Her-2/Neu and Chromosomal Aberrations in Breast Cancer. *Med J Armed Forces India*. 2008;64(1):11–5.
- Mudduwa LB. Quick score of hormone receptor status of breast carcinoma: Correlation with the other clinicopathological prognostic parameters. *Indian J Pathol Microbiol*. 2009;52(2):159–63.
- Ambroise M, Ghosh M, Mallikarjuna VS, Kurian A. Immunohistochemical Profile of Breast Cancer Patients at a Tertiary Care Hospital in South India. *Asian Pac J Cancer Prev*. 2011;12(3):625–9.
- James R, Thriveni K, Ramaswamy G, Krishnamoorthy L, Mukherjee G, Deshmane PPV, et al. Evaluation of immunohistochemistry and enzyme linked immunosorbent assay for HER-2/neu expression in breast carcinoma. *Indian J Clin Biochem*. 2008;23(4):345–51.
- Somasundaram K, Mukherjee G, Vaidyanathan K, Kumar P, Reddy CO, Deshmane V. ErbB-2 expression and its association with other biological parameters of breast cancer among Indian women. *Indian*

- Journal of Cancer*. 2010;47(1):8–15.
31. Song HS, Do YR, Kang SH, Jeong KY, Kim YS. Prognostic significance of immunohistochemical expression of p53 gene product in operable breast cancer. *Cancer Treat Res*. 2006;38(4):218–23.
 32. Sekar P, Bharti JN, Nigam JS, Sharma A, Soni PB. Evaluation of p53, HoxD10, and E-Cadherin Status in Breast Cancer and Correlation with Histological Grade and Other Prognostic Factors. *J Oncol*. 2014;doi:10.1155/2014/702527.
 33. Al-Joudi FS, Iskandar ZA, Rusli J. The expression of p53 in Invasive Ductal Carcinoma of the breast: A Study in the North-East States of Malaysia. *Med J Malaysia*. 2008;63:96–9.
 34. Rashed MM, Ragab NM, Galal MK. The association of HER-2/neu overexpression in relation to p53 nuclear accumulation, hormonal receptor status and common clinic-pathological prognostic parameters in a series of Egyptian women with invasive ductal carcinoma. *Eur J Gen Med*. 2007;4(2):73–9.
 35. Jr PR, Gammon MD, Zhang YJ, Terry MB, Hibshoosh H, Memeo L, et al. Mutations in p53, p53 protein overexpression and breast cancer survival. *J Cell Mol Med*. 2009;13(9b):3847–57.
 36. Cattoretti G, Rilke F, Andreola S, D'Amato L, Delia D. P53 expression in breast cancer. *Int J Cancer*. 1988;41(2):178–83.
 37. Jacquemier J, Molès JP, Penault-Llorca F, Adélaïde J, Torrente M, Viens P, et al. p53 immunohistochemical analysis in breast cancer with four monoclonal antibodies: comparison of staining and PCR-SSCP results. *Br J Cancer*. 1994;69(5):846–52.
 38. Nerurkar AV, Phulpagar MD, Shirsat NV, Ranade KJ. Expression of survivin and p53 proteins and their correlation with hormone receptor status in Indian breast cancer patients. *Indian J Med Sci*. 2009;63(11):481–90.
 39. Thor AD, Moore DH, Edgerton SM, Kawasaki ES, Reihnsaus E, Lynch HT, et al. Accumulation of p53 Tumor Suppressor Gene Protein: An Independent Marker of Prognosis in Breast Cancers. *J Natl Cancer Inst*. 1992;84(11):845–55.
 40. Rosen PP, Lesser ML, Arroyo CD, Cranor M, Borgen P, Norton L. p53 in node-negative breast carcinoma: an immunohistochemical study of epidemiologic risk factors, histologic features, and prognosis. *J Clin Oncol*. 1995;13(4):821–30.
 41. Han JS, Cao D, Molberg KH, Sarode VR, Rao R, Sutton LM, et al. Hormone Receptor Status Rather Than HER2 Status Is Significantly Associated With Increased Ki-67 and p53 Expression in Triple-Negative Breast Carcinomas, and High Expression of Ki-67 but Not p53 Is Significantly Associated With Axillary Nodal Metastasis in Triple-Negative and High-Grade Non-Triple-Negative Breast Carcinomas. *Am J Clin Pathol*. 2011;135(2):230–7.
 42. Lebe BA, Canda TÛ, Tuna BU, Sagol O, Ozer E. The evaluation of p53 and Ki67 expressions in invasive micropapillary carcinoma of the breast and its relation with other prognostic parameters: Thirty two cases. *Turk J Cancer*. 2002;32:48–62.
 43. Ivković-Kapicl T, Panjković M, Ninčić D, Knežević-Ušaj S. Factors correlating with lymph node metastases in patients with T1 ductal invasive breast cancer. *Archive*. 2006;14(1-2):19–22.
 44. Ding L, Zhang Z, Xu Y, Zhang Y. Comparative study of Her-2, p53, Ki-67 expression and clinicopathological characteristics of breast cancer in a cohort of northern China female patients. *Bioengineered*. 2017;8(4):383–92.
 45. Yamashita H, Nishio M, Toyama T, Sugiura H, Zhang Z, Kobayashi S, et al. Coexistence of HER2 over-expression and p53 protein accumulation is a strong prognostic molecular marker in breast cancer. *Breast Cancer Res*. 2003;6(1):24–30.

Author biography

Kriti Arora Junior Resident

Ruchee Khandelwal Professor

Hema Pant Professor

Cite this article: Arora K, Khandelwal R, Pant H. Evaluation of p53 in breast cancer and its correlation with various histological prognostic factors. *Indian J Pathol Oncol* 2020;7(3):392-398.