Research Article

# A comparative study of p53 expression in premalignant and malignant cervical lesions at a tertiary care institute of Rohilkhand region, India

**Vinay Yadav, Milan Jaiswal, Surabhi Pandey**

Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India

**Correspondence to:** Milan Jaiswal, E-mail: dr.milan.01@gmail.com

**Received:** December 25, 2017; **Accepted:** January 12, 2018

## ABSTRACT

**Background:** Cervical cancer ranks as the 2nd most common cancer among Indian women between 15 and 44 years of age. The secondary biomarker p53 has been studied at various centers in the world and has been found to be deregulated in cervical cancers. **Objective:** This study was undertaken to observe the expression and association of p53 and grades of p53 in premalignant and malignant cervical lesions and also with their histopathological subtypes. **Materials and Methods:** The present prospective study was conducted, from January 2016 to December 2016. Patients with premalignant and malignant cervical lesions of epithelial origin were included, while those with other pathological entities were excluded. A total of 53 patients were finally enroled for this study. Cases with p53 expression in more than 5% cells were considered positive for p53 overexpression. **Results:** The mean of p53 expression was higher in malignant lesions (13.29 ± 16.00) when compared to premalignant lesions (1.12 ± 2.23) and the result was statistically significant ($P$ = 0.019). No statistically significant association ($P$ = 0.875) was found between types of premalignant lesions and p53 overexpression as well as types of malignant lesions and p53 expression. **Conclusion:** In the present study, much higher percentage of p53 overexpression is observed in malignant than premalignant lesions, the difference being statistically significant ($P$ = 0.009). Mean p53 expression in the malignant lesions is also higher than premalignant lesions. p53 expression is therefore a suggested marker for differentiating malignant from premalignant lesions.

**KEY WORDS:** p53 Expression; Premalignant Cervical Lesion; Cervical Cancer

## INTRODUCTION

Cervical cancer ranks as the second most common cancer among Indian women between 15 and 44 years of age.[1] Unfortunately, over 70% of the cases of the cervical carcinoma present at a fairly advanced stage.[2] Current estimates indicate that, in India, every year approximately 1,23,000 women are diagnosed with cervical cancer, of which approximately 67,000 die from the disease. When comparing world cervical cancer crude incidence of 15.1, India has a higher crude incidence rate of 20.2 which is highest in Southern Asia. The Indian National Cancer Registry reported the highest crude rate of cervical cancers in Barshi, Maharashtra, and lowest in Sikkim, in India.[1]

There are two types of biomarkers in cervical cancers, i.e., primary and secondary. The primary biomarker is HPV DNA. The secondary biomarkers include tumor suppressor genes and proto-oncogenes (p53, p16, c-fos protein, Fra-1, RB- protein, telomerase, and Ki67), potential serum markers (squamous cell carcinoma antigen), cell adhesion matrix proteins (CD44), and miRNA.[3]

The secondary biomarker p53 has been studied at various centers in the world and has been found to be deregulated in cervical cancers. The p53 gene acts as tumor suppressor and

| Access this article online | |
|---|---|
| **Website:** http://www.ijmsph.com | **Quick: Response code** |
| **DOI:** 10.5455/ijmsph.2018.0100612012018 | |

is present on the short arm of chromosome 17 (17pl3.1).[4] It regulates proliferation of cells by promoting transcription of other genes controlling cell cycle.[5] The wild type of p53 gene helps in DNA repair by delaying the progression from G phase to the S phase of cell cycle.[6] This function is defective in the cells with mutant, stabilized, or inactivated p53 protein, and thus, these cells carry on replication of the abnormal DNA.[7] The inactivation of wild-type p53 gene is the most common genetic alteration in human carcinogenesis.[8] However, the results on p53 are quiet controversial; some workers have suggested the role of p53 in early carcinogenesis, while some others are of the opinion that p53 does not play an important role in carcinogenesis.[9-13]

Some studies have shown that the low expression of p53, in carcinoma cells before radiotherapy, is regarded as a predictive factor for good prognosis[13] and positive staining for p53 was associated with survival disadvantage.[12] Various authors have reported the variable expression of p53 in premalignant and malignant lesions of cervix.[9-10,12,14-16]

This study was undertaken to observe the expression and association of p53 and grades of p53 in premalignant and malignant cervical lesions and also with their histopathological subtypes.

## MATERIALS AND METHODS

The present prospective study was conducted in the Department of Pathology, at a tertiary care teaching institute of Rohilkhand region, from January 2016 to December 2016. Patients with premalignant and malignant cervical lesions of epithelial origin diagnosed on small biopsy or hysterectomy specimens were included, while those with other pathological entities were excluded. Cases with inadequate biopsy material were also excluded. A total of 53 patients were finally enroled for this study.

The cervical biopsy and hysterectomy specimens received were processed for routine paraffin embedding, and 3 to 5 μm thick sections were made from paraffin-embedded blocks. These sections were stained with hematoxylin and eosin (H and E) and also for p53 antibody (using polymer-based immunohistochemistry kit of BioGenx) along with appropriate positive controls. All microscopic slides were evaluated for histomorphological and immunohistochemical staining pattern by three independent observers blinded to the original histopathological diagnosis. P53 scoring was assessed by estimating the percentage of positively stained nuclei in fields of their maximum density with a 40× objective in 10 high-power fields. Cases with p53 expression in more than 5% cells were considered positive for p53 overexpression.[17]

Very few studies have utilized a grading system for p53 expression. In the present study, the following semiquantitative grading system for p53 expression was used.[18] Percentage of cells showing p53 expression was counted in 10 HPF and p53 expression was graded into five grades. Grade I (1% to 5% cells showing p53 expression), Grade II (6% to 25% cells showing p53 expression) Grade III (26% to 50% cells showing p53 expression), Grade IV (51% to 75% cells showing p53 expression), Grade V (more than 75% cells showing p53 expression).

Data pertaining to the age of patients, their histomorphological diagnosis, and p53 expression were compiled in structured pro forma and tabulated on Microsoft Excel spreadsheet (2007) and analyzed for descriptive statistics in terms of frequency, percentage, mean, and standard deviation (SD) for mean. Association/correlation of p53 expression in premalignant and malignant lesions was compared by applying Pearson's Chi-square test, Fisher's exact test, Yates' correction for continuity, *t*-test, and one-way ANOVA test, wherever applicable. Statistical analysis was performed using SPSS version 23 and $P < 0.05$ was considered statistically significant at 95% significance level.

## RESULTS

In the present study, of total 53 cases, majority, i.e., 84.91% of cases represented malignant lesions and only 15.09% of cases represented pre-malignant lesions. A largest number of cases were observed in the age range of 41–60 years comprising 54.72%, followed by age range of 21–40 years, comprising 32.08%. Only 13.21% of cases were observed in elderly females between 61 and 80 years. The mean age of presentation was 47.83, SD ± 10.53 years. Among premalignant lesions, 50.00% cases were present in the age range of 21–40 years and the rest 50.00% were present in age range 41–60 years. Among the malignant cases, the age range 41–60 years had a largest number of cases comprising 55.56%. A least number of malignant lesions were observed in the age range 61–80 years, while no premalignant lesion was observed in the same age group. The mean age of presentation for premalignant and malignant lesions was 41.00, SD ± 8.88 years and 49.04, SD ± 10.42 years, respectively. There was no statistically significant association ($P = 0.328$) between age range and premalignant/malignant lesions [Table 1].

Among the eight premalignant lesions, high-grade squamous intraepithelial lesion (HSIL) [Figure 1a] was more common comprising 87.50% of cases, while low-grade squamous intraepithelial lesion (LSIL) [Figure 1b] comprised only 12.50% of the premalignant cases. Among the malignant cases, only two histological types were observed, i.e., squamous cell carcinoma (SCC) [Figure 1d] and Adenocarcinoma [Figure 1c], SCC being more common, comprising 93.33% of the total malignant cases.

SCC and adenocarcinoma were more common in the age range of 41–60 years comprising 43.40% and 5.67% of total cases, respectively. The mean age of presentation for SCC and adenocarcinoma was 48.97, SD ± 10.56 years and 50.00, SD ± 10.00 years, respectively. There was no statistically significant association ($P$ = 0.910) between age range and types of malignant lesions [Table 2].

In the present study, 56.60% of cases were positive for p53 overexpression, while 43.40% were negative. Among the premalignant lesions, 12.50% of cases were positive for p53 overexpression, while among the malignant lesions, 64.44% were positive for p53 overexpression and the results were statistically significant ($P$ = 0.009). The mean of p53 expression was higher in malignant lesions (13.29 ± 16.00) when compared to premalignant lesions (1.12 ± 2.23), and the result was statistically significant ($P$ = 0.019) [Table 3].

Among the HSIL, only 14.29% were positive for p53 overexpression [Figure 2a] while among the LSIL not a single case was positive for p53 overexpression [Figure 2b]. No statistically significant association ($P$ = 0.875) was found between types of pre-malignant lesions and p53 overexpression.

Among the cases of SCCs, 66.67% were positive for p53 overexpression [Figure 2d], while among the cases of adenocarcinoma, 33.33% were positive [Figure 2c]. Comparing p53 overexpression in the two groups, the result was not statistically significant ($P$ = 0.285) [Table 4].

Maximum cases were positive for p53 overexpression in the age range 61–80 years comprising 85.71%. A least number of cases were positive for p53 overexpression in the age range 41–60 years comprising 51.72%. Comparing the three groups for p53 overexpression, no statistically significant result was observed ($P$ = 0.248). The mean of p53 expression among age range 21–40 years, 41–60 years, and 61–80 years was almost same, i.e. 11.23 ± 17.48, 10.69 ± 14.26, and 15.14 ± 16.48, respectively, and the results were not statistically significant ($P$ = 0.794) [Table 5].

Among all the cases, maximum number of cases belonged to Grade II of p53 expression comprising 55.00%. Not a single case was observed in the Grade V of p53 expression. Cases with no nuclear staining or with <1% p53 expression were not graded ($n$ = 13). In the present study, only one case of premalignant lesion was observed in each Grade I and Grade II of p53 expression comprising 50.00% of cases. Among malignant lesions, majority of cases were observed in Grade II of p53 expression, comprising 55.26% of cases followed by Grade I of p53 expression, comprising 23.68%. The results were not statistically significant ($P$ = 0.355) when p53 grades were compared with pre-malignant/ malignant lesions. Cases with no nuclear staining or <1%

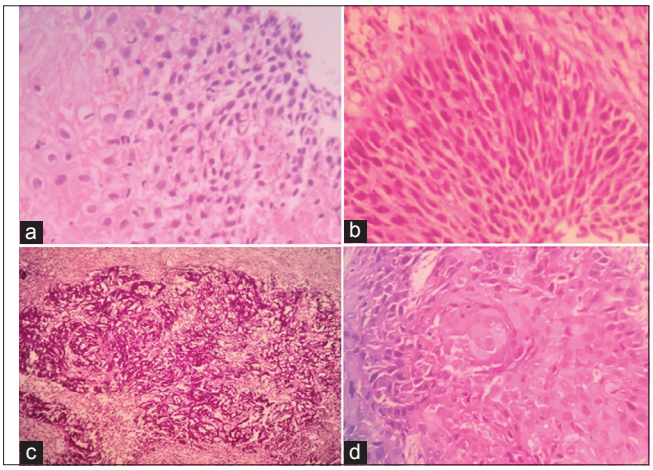


**Figure 1:** H and E stained photomicrographs showing: (a) - High-grade squamous intraepithelial lesion, (b) – low-grade squamous intraepithelial lesion, (c) - adenocarcinoma, (d) - squamous cell carcinoma

**Table 1:** Distribution of premalignant and malignant lesions with respect to age range

| Age range (years) | *n* | | |
|---|---|---|---|
| | Premalignant | Malignant | Total cases |
| (21–40) | 4 | 13 | 17 |
| (41–60) | 4 | 25 | 29 |
| (61–80) | 0 | 7 | 7 |
| Total | 8 | 45 | 53 |

**Table 2:** Distribution of types of premalignant and malignant lesions with respect to age range

| Age range (years) | *n* | | | |
|---|---|---|---|---|
| | LSIL | HSIL | SCC | Adenocarcinoma |
| (21–40) | 0 | 4 | 12 | 1 |
| (41–60) | 1 | 3 | 23 | 2 |
| (61–80) | 0 | 0 | 7 | 0 |
| Total | 1 | 7 | 42 | 3 |

HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intraepithelial lesion, SCC: Squamous cell carcinoma

**Table 3:** Frequency distribution of premalignant and malignant lesions with respect to P53 overexpression

| P-53 overexpression | *n* | | |
|---|---|---|---|
| | Pre-malignant | Malignant | Total cases |
| Positive | 1 | 29 | 30 |
| Negative | 7 | 16 | 23 |
| Total | 8 | 45 | 53 |

HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intraepithelial lesion, SCC: Squamous cell carcinoma

p53 expression were not graded, comprising six and seven cases of premalignant and malignant lesions, respectively [Figure 3].

One case of HSIL was observed in Grade I and Grade II of p53 expression comprising 50.00% of cases each. Among LSIL, not a single case was graded for p53 expression. The results were not statistically significant ($P = 0.832$) when p53 grades were compared with types of premalignant lesions. Cases with no nuclear staining or <1% p53 expression were not graded, comprising five cases and one case of HSIL and LSIL, respectively. Among the cases of SCCs, most belonged to Grade II of p53 expression, comprising 60.00% followed by Grade I of p53 expression comprising 20.00%. Not a single case of SCC was observed in Grade V of p53 expression. Among adenocarcinomas, maximum number of cases belonged to the Grade II of p53 expression, comprising 66.67% of cases, followed by Grade III of p53 expression, comprising 33.33%. The results were not statistically significant ($P = 0.703$) when p53 grades were compared with the histological type of malignant lesions. Cases of SCC with no nuclear staining or <1% p53 expression were not graded, comprising seven cases [Figure 4].

## DISCUSSION

p53 is a biological marker deregulated in cervical malignancies and variably expressed in premalignant and malignant lesions as reported in various studies.[9-10,12,14-16] In the present study, a total of 53 cases were enrolled, majority being malignant (84.91%). Common histological types among malignant and premalignant lesions were HSIL and SCC, respectively. The mean age of presentation was 47.83, SD ± 10.53 years, and majority cases were observed in the age range of 41–60 years. The mean age of presentation for malignant lesions (49.04, SD ± 10.42 years) was slightly higher than that of premalignant lesions (41.00, SD ± 8.88 years). With respect to the age of presentation, no statistically significant association was observed for both pre-malignant and malignant lesions. A greater proportion of malignant lesions (64.44%) were positive for p53 overexpression when compared to premalignant lesions (12.50%). The mean of p53 expression among premalignant and malignant lesions was statistically significant ($P = 0.019$). The mean of p53 expression among various histological types of premalignant and malignant lesions was not statistically significant. Among all the cases, largest number of cases belonged to Grade II of p53 expression while not a single case was observed in the Grade V of p53 expression.

SCC was observed as the most common cervical malignancy comprising 93.33% of cases, in the present study, distribution almost being similar to that reported by Lo *et al*.[19] (90.4%), Raza *et al*.[20] (86.8%), and Siddiqa *et al*.[21] (91.5%). However, in a study done by Gul *et al*.,[22] the proportion of SCCs was comparatively less, i.e., 58.9%. SCCs are the most common histological type as the most common etiological agent responsible for cervical cancer is HPV which most commonly affects the lining cervical[19,23] epithelium. HSIL was the common histological subtype in premalignant lesions in the present study which is in concordance to the studies done by Jeffers *et al*.[24]

The mean age of presentation of malignant lesions (49.04 ± 10.42 years) is almost similar to that reported by Rajaram *et al*.[25] (52.1 ± 12.46 years), Tan *et al*.[26] (51.1 years), Koncar *et al*.[27] (50 years), and Tan *et al*.[28] (50.3 years). Furthermore, the mean age of presentation of premalignant lesions (41.00 ± 8.89 years) is younger than that of malignant lesions. These findings are in concordance with that reported by Tan *et al*.[26] and Tan *et al*.[28] For

**Table 4:** Frequency distribution of premalignant and malignant lesions with respect to P53 overexpression

| P 53 Overexpression | *n* | | | |
|---|---|---|---|---|
| | HSIL | LSIL | SCC | Adenocarcinoma |
| Positive | 1 | 0 | 28 | 1 |
| Negative | 6 | 1 | 14 | 2 |
| Total | 7 | 1 | 42 | 3 |

HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intraepithelial lesion, SCC: Squamous cell carcinoma

**Table 5:** Frequency distribution of age ranges with respect to P53 overexpression

| Age range | *n* | | |
|---|---|---|---|
| | (21–40) | (41–60) | (61–80) |
| Positive | 9 | 15 | 6 |
| Negative | 8 | 14 | 1 |
| Total | 17 | 29 | 7 |

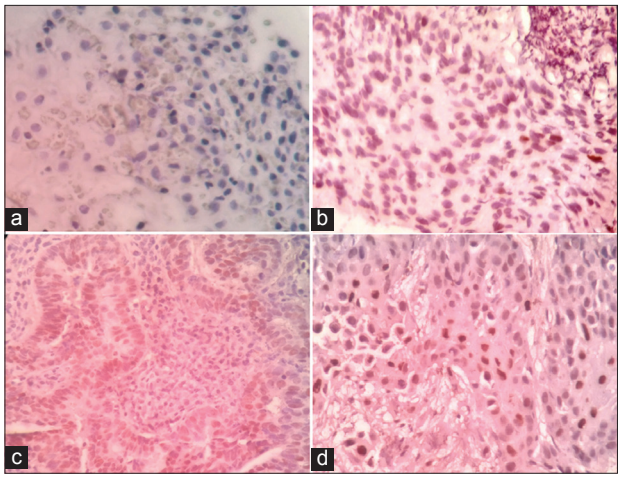


**Figure 2:** p53 immunohistochemistry stained photomicrographs showing: (a) - High-grade squamous intraepithelial lesion, (b) - low-grade squamous intraepithelial lesion, (c) - adenocarcinoma, (d) - squamous cell carcinoma

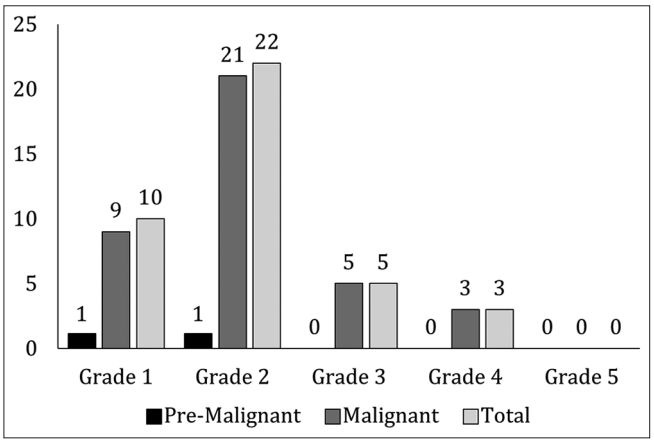


**Figure 3:** Frequency distribution of premalignant and malignant lesions with respect to various grades of p53 expression

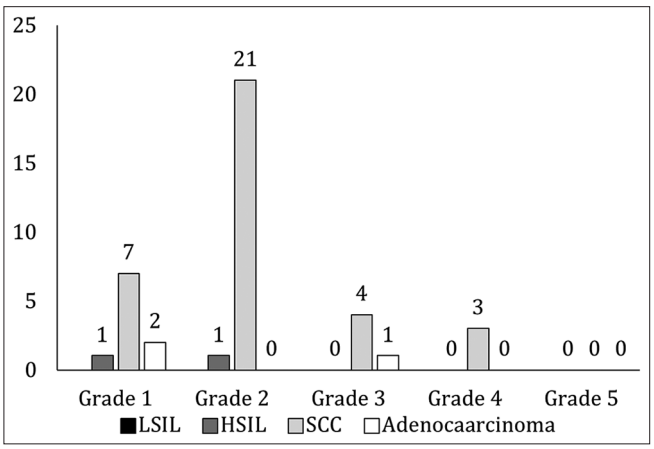


**Figure 4:** Frequency distribution of types of premalignant and malignant lesions with respect to various grades of p53 expression

malignant lesions, Ikuta *et al*.[29] reported a statistically significant correlation ($P$ = 0.02) between p53 expression and age; however, no significant association was observed in the present study ($P$ = 0.473) for either malignant or premalignant lesion warranting further studies with larger sample size to be undertaken to ascertain correlation of age with p53 expression in cervical lesions.

The mean of p53 expression among premalignant and malignant lesions, in the present study, was statistically significant which is in concordance to studies done by Anwar *et al*.,[9] Giarnieri *et al*.,[14] and Baskaran *et al*.,[30] thus supporting the view that p53 plays a role in carcinogenesis. In cervical cancers, variable p53 overexpression in cervical cancer has been reported by various authors[9-10,12,14-16] ranging from 17.1% by Hunt *et al*.[10] to 75.9% by Anwar *et al*.[9] In the present study, p53 overexpression was observed in 64.44% of cases of carcinoma cervix. One case of HSIL was positive for p53 overexpression. In comparison to the normal cervical epithelium, the pattern of staining was different. In HSIL, the p53-positive cells were present throughout the layers of lining epithelium as compared to normal cervical epithelium, wherein the p53 positivity was present in only basal layers of the squamous epithelium. Similar pattern of positivity was observed by Jeffers *et al*.[24]

Studies done by Lindström *et al*.[31] and Bahnassy *et al*.[32] observed a statistically significant relation between histological type of cervical cancer and p53 overexpression. However, in the present study, no statistically significant relation was observed because of small sample size and still lesser sample size of adenocarcinomas. Among malignant lesions, a higher percentage of SCC (66.7%), were positive for p53 overexpression as seen in various studies done by Tjalma *et al*.[17] (83.0%), Tan *et al*.[26] (94.4%) and Tan *et al*.[28] (72.2%). P53 overexpression was seen in 33.3% of cases of adenocarcinoma similar to that seen in a study done by Lindström *et al*.[31] (33.3%), whereas in a study done by Hunt *et al*.,[10] p53 overexpression was reported in only 14.3% of cases of adenocarcinoma.

In the present study, no statistical significant association was observed when p53 grades were compared with premalignant and malignant lesions as well as with their histological subtypes. Very few studies, such as a done by Win *et al*.,[18] have compared the grades of p53 expression in premalignant and malignant cervical lesions, but not a single study has evaluated the statistical significance between the two. Further studies to evaluate the association of histological types and grade of cervical lesions with respect to grades of p53 expression are warranted for conclusive discussions.

In the present study, an attempt was made to evaluate to grade of p53 expression with histological type of premalignant and malignant lesions. However, no statistical significant results were obtained because of the small sample size of the individual lesions. Although statistically insignificant results are obtained for HSIL, LSIL, and adenocarcinoma, the present study cannot definitely comment on their probability of association with p53 expression because of their small individual sample size; therefore, this necessitates follow-up studies with a larger sample size.

## CONCLUSION

In the present study, much higher percentage of p53 overexpression is observed in malignant than premalignant lesions, the difference being statistically significant ($P$ = 0.009). Mean p53 expression in the malignant lesions is also higher (13.29 ± 16.00) than premalignant lesions (1.12 ± 2.23). P53 expression is, therefore, a suggested marker for differentiating malignant from premalignant lesions.

## REFERENCES

1. Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gómez D, *et al.* Human Papillomavirus and Related Diseases in

India-Report. ICO Information Centre on HPV and Cancer (HPV Information Centre); 2015. Available from: http://www.hpvcentre.net/statistics/reports/IND.pdf. [Last cited on 2017 Jul 18].
2. Nandakumar A, Anantha N, Venugopal TC. Incidence, mortality and survival in cancer of the cervix in Bangalore, India. Br J Cancer 1995;71:1348-52.
3. Indian Council of Medical Research. Consensus Document for The Management of Cancer Cervix. New Delhi: Indian Council of Medical Research; 2016. Available from: http://www.screening.iarc.fr/doc/WHO_India_CCSP_guidelines_2005.pdf. [Last cited on 2017 Jul 18].
4. Levine AJ, Momand J, Finlay CA. The p53 tumour suppressor gene. Nature 1991;351:453-6.
5. Finlay CA, Hinds PW, Levine AJ. The p53 proto-oncogene can act as a suppressor of transformation. Cell 1989;57:1083-93.
6. Hollstein M, Sidransky D, Vogelstein B, Harris CC. P53 mutations in human cancers. Science 1991;253:49-53.
7. Bartek J, Bartkova J, Vojtesek B, Stakova Z, Lukas J, Rejthar A, *et al*. Aberrant expression of the p53 oncoprotein is a common feature of a wide spectrum of human malignan-cies. Oncogene 1991;6:1699-703.
8. Levine AJ, Perry ME, Chang A, Silver A, Dittmer D, Wu M, *et al*. The 1993 walter hubert lecture: The role of the p53 tumour suppressor gene in tumorigenesis. Br J Cancer 1994;69:409-16.
9. Anwar K, Nakakuki K, Imai H, Shiraishi T, Inuzuka M. Infection of human papillomavirus (HPV) and p53 over-expression in human female genital tract carcinoma. J Pak Med Assoc 1996;46:220-4.
10. Hunt CR, Hale RJ, Buckley CH, Hunt J. P53 expression in carcinoma of the cervix. J Clin Pathol 1996;49:971.
11. Tenti P, Pavanello S, Padovan L, Spinillo A, Vesentini N, Zappatore R, *et al.* Analysis and clinical implications of p53 gene mutations and human papillomavirus Type 16 and 18 infection in primary adenocarcinoma of the uterine cervix. Am J Pathol 1998;152:1057-63.
12. Crawford RA, Caldwell C, Iles RK, Lowe D, Shepherd JH, Chard T, *et al.* Prognostic significance of the bcl-2 apoptotic family of proteins in primary and recurrent cervical cancer. Br J Cancer 1998;78:210-4.
13. Oka K, Suzuki Y, Nakano T. Expression of p27 and p53 in cervical squamous cell carcinoma patients treated with radiotherapy alone: Radiotherapeutic effect and prognosis. Cancer 2000;88:2766-73.
14. Giarnieri E, Mancini R, Pisani T, Alderisio M, Vecchione A. Msh2, mlh1, fhit, p53, bcl-2, and bax expression in invasive and *in situ* squamous cell carcinoma of the uterine cervix. Clin Cancer Res 2000;6:3600-6.
15. Vasilescu F, Ceauşu M, Tănase C, Stănculescu R, Vlădescu T, Ceauşu Z, *et al.* P53, p63 and ki-67 assessment in HPV-induced cervical neoplasia. Rom J Morphol Embryol 2009;50:357-61.
16. Shukla S, Dass J, Pujani M. P53 and bcl2 expression in malignant and premalignant lesions of uterine cervix and their correlation with human papilloma Virus 16 and 18. South Asian J Cancer 2014;3:48-53.
17. Tjalma WA, Weyler JJ, Bogers JJ, Pollefliet C, Baay M, Goovaerts GC, *et al.* The importance of biological factors (bcl-2, bax, p53, PCNA, MI, HPV and angiogenesis) in invasive cervical cancer. Eur J Obstet Gynecol Reprod Biol 2001;97:223-30.
18. Win N, Thu TM, Tun AN, Aye TT, Soe S, Nyunt K, *et al*. P53 expression in carcinoma cervix. Myanmar Med J 2004;48:1-4.
19. Lo KW, Wong YF, Chan MK, Li JC, Poon JS, Wang VW, *et al.* Prevalence of human papillomavirus in cervical cancer: A multicenter study in China. Int J Cancer 2002;100:327-31.
20. Raza SA, Franceschi S, Pallardy S, Malik FR, Avan BI, Zafar A, *et al.* Human papillomavirus infection in women with and without cervical cancer in Karachi, Pakistan. Br J Cancer 2010;102:1657-60.
21. Siddiqa A, Zainab M, Qadri I, Bhatti MF, Parish JL. Prevalence and genotyping of high risk human papillomavirus in cervical cancer samples from Punjab, Pakistan. Viruses 2014;6:2762-77.
22. Gul S, Murad S, Javed A. Prevalence of high risk human papillomavirus in cervical dysplasia and cancer samples from Twin cities in Pakistan. Int J Infect Dis 2015;34:14-9.
23. Unger ER, Barr E. Human papillomavirus and cervical cancer. Emerg Infect Dis 2004. Available from: http://www.dx.doi.org/10.3201/eid1011.040623_09. [Last cited on 2017 Jul 21].
24. Jeffers MD, Richmond J, Farquharson M, McNicol AM. P53 immunoreactivity in cervical intraepithelial neoplasia and non neoplastic cervical squamous epithelium. J Clin Pathol 1996;47:1073.
25. Rajaram S, Gupta G, Agarwal S, Goel N, Singh KC. High-risk human papillomavirus, tumor suppressor protein p53 and mitomycin-C in invasive squamous cell carcinoma cervix. Indian J Cancer 2006;43:156-62.
26. Tan GC, Sharifah NA, Shiran MS, Salwati S, Hatta AZ, Paul-Ng HO, *et al.* Utility of ki-67 and p53 in distinguishing cervical intraepithelial neoplasia 3 from squamous cell carcinoma of the cervix. Asian Pac J Cancer Prev 2008;9:781-4.
27. Koncar RF, Feldman R, Bahassi EM, Hashemi Sadraei N. Comparative molecular profiling of HPV-induced squamous cell carcinomas. Cancer Med 2017;6:1673-85.
28. Tan GC, Sharifah NA, Salwati S, Shiran MS, Hatta AZ, Ng HO. Immunohistochemical study of p53 expression in premalignant and malignant cervical neoplasms. Med Health 2007;2:125-32.
29. Ikuta A, Saito J, Mizokami T, Nakamoto T, Yasuhara M, Nagata F, *et al.* Correlation p53 expression and human papilloma virus deoxyribonucleic acid with clinical outcome in early uterine cervical carcinoma. Cancer Detect Prev 2005;29:528-36.
30. Baskaran K, Karunanithi S, Sivakamasundari I, Sundresh J, Thamaraiselvi B, Swaruparani S. Overexpression of p53 and its role as early biomarker in carcinoma of uterine cervix. Int J Res Pharm Sci 2013;4:198-202.
31. Lindström AK, Tot T, Stendahl U, Syrjänen S, Syrjänen K, Hellberg D, *et al.* Discrepancies in expression and prognostic value of tumor markers in adenocarcinoma and squamous cell carcinoma in cervical cancer. Anticancer Res 2009;29:2577-8.
32. Bahnassy AA, Zekri AR, Saleh M, Lotayef M, Moneir M, Shawki O, *et al.* The possible role of cell cycle regulators in multistep process of HPV-associated cervical carcinoma. BMC Clin Pathol 2007;7:4.

**How to cite this article:** Yadav V, Jaiswal M, Pandey S. A comparative study of p53 expression in premalignant and malignant cervical lesions at a tertiary care institute of Rohilkhand region, India. Int J Med Sci Public Health 2018;7(3):216-221.

**Source of Support:** Nil,**Conflict of Interest:** None declared.