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Original article

EVALUATION OF ROLE OF HER2 EXPRESSION BY IHC IN PREMALIGNANT AND MALIGNANT LESIONS OF THE UTERINE CERVIX – AN INSTITUTIONAL BASED PROSPECTIVE STUDY.

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Abstract

Background:

The most frequent malignancy in Indian women is uterine cervix cancer. According to the clinical stage of the tumour and the surgical findings, surgery is the primary mode of treatment, coupled with radiation and chemotherapy. Despite the use of cisplatin-based combination treatment, patients with advanced or recurring illness have a poor prognosis. In order to replace or supplement the present therapy for these patients, it is becoming more and more important to identify novel therapeutic targets. The goal of the current investigation was to determine whether Her-2/neu expression was present.

Methods:

In this investigation, 81 cervical specimens were used. These cases included squamous cell carcinoma and adenocarcinoma diagnoses. BioGenex monoclonal mouse anti-human HER-2/neu Receptor IgG1 antibody was used for HER-2/neu immunostaining.

Results:

Malignant lesions showed higher expression of HER-2/neu compared to premalignant lesions. Additionally, there was a correlation between staining intensity and lymph node metastasis, clinical stage, and malignant tumour grade.

Conclusion:

Oncoprotein HER-2/neu overexpression has been linked to aggressive biological behaviour, a poor prognosis, and the propensity for metastatic spread.

Keywords: Cervical carcinoma, Immunohistochemistry, Oncoprotein, Overexpression, Submitted: 2023-06-22 Accepted: 2023-06-25

1. Introduction:

In the world-wide distribution of cancer among females "Cervical cancer / Cancer Cervix" ranks the fourth most common malignancy in the incidence and mortality [1]. The Global burden can be well appreciated from the figures that, in 2018 the number of new cases of carcinoma cervix was 569847 and the resultant deaths was 311365 [1]. In developing country like India Carcinoma of uterine cervix is the 2nd most prevalent cancer and ranks 3rd in mortality from cancer [2]. The incidence rate of carcinoma cervix in India is 9 to 44 per 100,000 women [3]. As the current

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treatment modalities are failing to cure locally advanced disease, the necessity of development of a molecular targeted therapy to improve the outcome in such cases arises [4]. The c-erbB-2 proto-oncogene, also called HER-2/neu, is located on Chromosome 17q21 which encodes 185kDa transmembrane glycoprotein with tyrosine kinase activity. Overexpression leads to constitutive activation of tyrosine kinase residues [5]. The epidermal growth factor receptor (EGFR/HER) family of receptors has been associated with aggressive biological behavior and metastatic potential [6]. The established role of Her2/neu status evaluation in treating the subset of Her2/neu positive breast cancers with targeted molecular treatment using Transtuzumab has invoked researchers to study its role in other malignancies including cervical carcinomas. The expression of HER family members in gynecological cancers and their relationship with disease stage, grade and response to treatment remains controversial [7]. The present study was undertaken to assess the relationship of Her2/neu expression with other prognostic parameters in cervical malignancies.

1.1. Aims & Objectives:

The present study was conducted with an aim to study the expression pattern of Her2/neu in the various pre-malignant and malignant lesions of the uterine cervix by immunohistochemistry and to assess its relationship with other prognostic parameters like tumor type, histological grade, parametrial involvement & lymph node involvement.

2. Materials & Methods:

A cross sectional prospective study of 2 years duration was conducted in the Department of Pathology, MKCG MCH Brahmapur, Odisha, India after obtaining the approval of the Institutional Ethical Committee. This study was conducted between May 2020 to May 2022 with a sample size of 81 patients. Inclusion criteria was all types of biopsy samples from cervix received in the department. Exclusion criteria was lack of informed consent and patients with recurrent carcinoma cervix. Detailed clinical history & examination findings along with other relevant investigation findings were recorded in each case. Routine H&E slides were evaluation and the diagnoses were recorded. Her2/neu status was evaluated by using IHC using DakoHercept test polyclonal antibody.Her2/neu expression was graded as per the ASCO/CAP guidelines 2014:

TABLE – 1: ASCO/CAP guidelines 2014

Intensity of HER-2 expression	Characteristic features
0	No staining is observed or shows membrane staining that is incomplete and is faint/barely perceptible and within <10% of tumor cells.
1+	Membrane staining that is incomplete and is faint/barely perceptible and within >10% of tumor cells.
2+	Circumferential staining that is incomplete and/or weak/moderate within > 10% of tumor cells or complete intense circumferential membrane staining within < 10% of tumor cells.
3+	Complete intense circumferential membrane staining within > 10% of tumor cells.

Statistical analysis was done using SPSS version 18 and a p value of <0.05 was considered to be significant.

2.1. Observations:

In the present study, maximum number of cases were recorded between 41 to 60 years accounting for 63 cases [77.78%].

TABLE –2: AGE DISTRIBUTION OF CASES. [n=81]

Age in years	Number of patients	Percentage
31-40	4	4.93
41-50	26	32.10
51-60	37	45.68
61-70	12	14.82
> 70	2	2.47
Total	**81**	**100**

Present study observed a prevalence of carcinoma cervix in the postmenopausal age group accounting for two-third cases i.e. 54 cases.

TABLE –3: MENSTRUAL STATUS OF PATIENTS. [n = 81]		
Menstrual status(Age in yrs.)	**Number of patients**	**Percentage**
Reproductive (20-49)	27	33.33
Postmenopausal (>50)	54	66.67
Total	**81**	**100**

The clinical presentation at diagnosis were varied with bleeding per vaginum being the most common manifestation found in 39 cases [48.14%].

TABLE –4: CLINICAL PRESENTATIONS. [n = 81]		
Complaints of	**Number of cases**	**Percentage**
Bleeding P/V	39	48.14
Foul smelling dischargeP/V	10	12.35
Backache	08	9.88
Retention of urine	17	20.99
Abdominal mass & fever (pyometra)	03	3.70
Accidental discovery - Anemia, Loss of appetite	4	4.94
Total	**81**	**100**

Premalignant lesion i.e. CIN was diagnosed in 11 cases [13.58%] and malignancy in 70 cases [86.42%]. Of the malignant cases Squamous cell carcinoma was commonest accounting for 58 cases [82.86%].

TABLE –5: CASE DISTRIBUTION OF LESIONS. [n = 81]		
Type of lesion	**Number of cases**	**Percentage**
CIN	11	13.58
Squamous cell carcinoma	58	71.61
Adenocarcinoma	12	14.81
Total	**81**	**100**

TABLE – 6: HISTOLOGICAL GRADES OF SQUAMOUS CELL CARCINOMA. [n = 58]		
Grade	**Number of cases**	**Percentage**
Well differentiated	8	13.80
Moderately differentiated	40	68.96
Poorly differentiated	10	17.24
Total	**58**	**100**

TABLE – 7: HISTOLOGICAL GRADES OF ADENOCARCINOMA. [n = 12]		
Grade	**Number of cases**	**Percentage**
Well differentiated	3	25
Moderately differentiated	9	75
Poorly differentiated	0	0
Total	**12**	**100**

Premalignant lesion i.e. CIN was diagnosed in 11 cases [13.58%] and malignancy in 70 cases [86.42%]. Of the malignant cases Squamous cell carcinoma was commonest accounting for 58 cases [82.86%].

Majority of the squamous cell carcinomas were graded histopathologically to Grade 2 i.e. moderately differentiated, 40 cases [68.96%].

Similarly, majority of adenocarcinomas were graded histopathologically to Grade 2 i.e. moderately differentiated, 9 cases [75%]. Not a single case of poorly differentiated adenocarcinoma was encountered in the study.

In the 70 cases of Warthim's resection for carcinoma cervix, 25 cases showed lymph node metastases accounting for 35.72% cases.

Clinical staging was possible in 72 cases and Stage III was the most prevalent, 25 cases [34.72%] followed by Stage I & Stage II, 22 cases [30.56%] and 20 cases [27.78%] respectively.

TABLE – 9: CLINICAL STAGE AT PRESENTATION. [n = 72]		
Stage	**Number of cases**	**Percentage**
0	2	2.78
I	22	30.56
II	20	27.78
III	25	34.72
IV	3	4.17
Total	**72**	**100**

On evaluation of the Her-2/neu expression pattern it was observed that: [i] none of the CIN cases were found to be positive; [ii] among the SCC and Adenocarcinoma of cervix cases, there was significantly higher expression of Her-2/neu, 66.66% in contrast to 31.03% in SCC cervix cases.

TABLE – 10: STAINING PATTERN OF HER-2/NEU IN VARIOUS LESIONS. [n = 81]						
Intensity of staining of HER-2	**CIN**	**SCC**	**Adenoca**	**Total**	**Percentage**	**p Value**
0 (Negative)	5	12	0	17	20.99	0.0023
1+(Negative)	5	13	0	18	22.22	
2+(Equivocal)	1	15	4	20	24.69	
3+(Positive)	0	18	8	26	32.10	

10 out of the total 11 cases of CIN are negative for Her-2/neu expression and only one showed equivocal staining. None of the cases showed definite positivity.

TABLE – 11: EXPRESSION PATTERN OF HER-2/NEU IN CIN [n = 11]						
CIN	**Number of cases**	**HER-2 Expression**				**p-Value**
		3+	**2+**	**1+**	**0**	
LSIL	9	0	0	4	5	0.0601
HSIL	2	0	1	1	0	
Total	**11**	**0**	**1**	**5**	**5**	

A statistically significant pattern of expression of Her-2/neu was observed in cases of SCC cervix that the rate of Her-2/neu positivity in inversely proportional to the degree of differentiation of the tumor as is evident from the facts that, [i] none of the well differentiated SCC cases were positive or equivocal; [ii] 25% cases of moderately differentiated SCC cases were positive and 32.5% cases were equivocal and [iii] 80% of poorly differentiated SCC cases were positive and rest 20% cases were equivocal in Her-2/neu expression. These observations are statistically significant. [p value – 0.004].

TABLE – 12: EXPRESSION PATTERN OF HER-2/NEU IN SCC [n = 58]						
Histologic grade	**Number of cases**	**HER-2 Expression**				**p Value**
		3+	**2+**	**1+**	**0**	
Well differentiated	8	0	0	5	3	0.004
Moderately differentiated	40	10	13	8	9	
Poorly Differentiated	10	8	2	0	0	
Total	**58**	**18**	**15**	**13**	**12**	
Percentage	**100**	**31.03**	**25.87**	**22.41**	**20.69**	

On evaluation of the Her-2/neu expression pattern it was observed that: [i] none of the CIN cases were found to be positive; [ii] among the SCC and Adenocarcinoma of cervix cases, there was significantly higher expression of Her-2/neu, 66.66% in contrast to 31.03% in SCC cervix cases.

In cases of Adenocarcinoma of cervix, a Her-2/neu expression pattern similar to SCC cervix was observed i.e. the degree of expression was inversely proportional to the degree of differentiation with a limitation that there was no poorly differentiated case was encountered in the study. 100% of well differentiated Adenocarcinomas were equivocal in Her-2/neu expression and 88.88% of moderately differentiated ones were positive for Her-2/neu expression, the remaining 11.11% cases of moderately differentiated type were equivocal.

TABLE – 13: EXPRESSION PATTERN OF HER-2/NEU IN ADENOCA [n = 12]						
Histologic grade	**Number of cases**	**HER-2 Expression**				**p Value**
		3+	**2+**	**1+**	**0**	
Well differentiated	3	0	3	0	0	0.0182
Moderately differentiated	9	8	1	0	0	
Poorly Differentiated	0	0	0	0	0	
Total	**12**	**8**	**4**	**0**	**0**	
Percentage	**100**	**66.67**	**33.33**	**0**	**0**	

When Her-2/neu expression pattern was corelated with the stage at diagnosis, the present study observed that, the degree of expression was directly proportional to the stage of the disease i.e. as the stage advances the Her-2/neu positivity also increases. This is evident from the facts that, [i] none of the Stage 0 cases showed positivity; [ii] only 4.54% of Stage 1 cases were positive; [iii] the positivity shoots up to 30% for Stage 2 cases, 64% for Stage 3 cases and 100% of Stage 4 cases. The observations made are statistically significant [p value – 0.0001].

TABLE – 14: EXPRESSION PATTERN OF HER-2/NEU IN RELATION TO CLINICAL STAGE AT PRESENTATION [n = 72]						
Stage	**Number of cases**	**HER-2 Expression**				**p Value**
		3+	**2+**	**1+**	**0**	
0	2	0	2	0	0	<0.0001
1	22	1	4	8	9	
2	20	6	9	3	2	
3	25	16	6	2	1	
4	3	3	0	0	0	
Total	**72**	**26**	**21**	**13**	**12**	
Percentage	**100**	**36.11**	**29.17**	**18.06**	**16.67**	

On comparing the Her-2/neu expression pattern with lymph node metastasis status, the present study observed that the expression was statistically significantly higher for Her-2/neu positive status when the metastasis to lymph node is present, 68% cases with metastases showed positivity in comparison to 20% positivity in the absence of metastases [p value – 0.0004].

TABLE – 15: EXPRESSION PATTERN OF HER-2/NEU IN RELATION TO LYMPH NODE METASTASES. [n = 70]						
Metastasis	**Number of cases**	**HER-2 Expression**				**p Value**
		3+	**2+**	**1+**	**0**	
Present	25	17	5	3	0	0.0004
Absent	45	9	14	10	12	
Total	**70**	**26**	**19**	**13**	**12**	
Percentage	**100**	**37.14**	**27.14**	**18.57**	**17.14**	

3. Discussion:

Cancer of the uterine cervix, the most prevalent cancers among the Indian females is an important cause of morbidity and mortality among women [8]. It is more common in the perimenopausal age group. Among the malignant lesions of the cervix, squamous cell carcinoma is the most common in its prevalence followed by adenocarcinomas & adenosquamous carcinomas. Currently, extensive studies have been conducted on the expression pattern of the oncogene, c-erb-2/HER-2, in the various tumors of the breast, ovary, endometrium, cervix, fallopian tube, etc [9]. The exact function of HER-2/neu gene product is still unknown, but it has been documented to have tyrosine kinase activity and is thought to function as receptor for growth-regulating molecules. Overexpression and/or mutation of HER-2/neu results in quantitative and qualitative alteration in the membrane proteins which is the basis of its detection [10, 11]. Many studies have suggested that amplification or over-expression of the oncogene might be a marker of poor prognosis in cancers of the ovary, endometrium, breast etc [12-14]. There have been reports in the literature that c-erbB-2 over-expression correlates with reduced benefit of adjuvant therapy as in cases of carcinoma breast with tamoxifen therapy.[15,16] Many studies have convincingly shown that regression of c-erbB-2 suppresses the malignant phenotypes of cancer cells. Over-expressing this oncoprotein, may serve as an excellent target for developing anti-cancer agents [17]. HER-2 overexpression can be estimated either by detection of gene amplification by fluorescent in situ hybridization (FISH) or immunohistochemical method. Intensity of HER-2 expression is graded as 0,1+,2+ & 3+ according to the 2014 ASCO/CAP guidelines. Some authors stress that the cases with moderate intensity (2+) staining require complementary FISH, to verify gene amplification. This combination is not necessary for low (0 / 1+) or high (3+) grades of immunohistochemical stain because the correlation with gene amplification status is acceptably high [18].

The mean age at presentation in the present study for CIN cases was 43 years (37 – 51 years) and the same for invasive malignancies was 55.04 years (43 – 72 years). Similar finding i.e. the mean age at presentation in cases of CIN and invasive malignancy was observed to be 49years & 53.75 years in the study conducted by Wyatt et al [10].

The commonest histological subtype encountered in the present study was SCC cervix (71.6% cases) followed by Adenocarcinoma of cervix (14.82% cases) and CIN (13.58% cases). Most of the studies have observed a similar prevalence of

histological subtypes except the study of Joseph et al who found a higher prevalence of CIN in their study.

On assessing the prevalence of histological grade of the SCC of cervix cases, the present study found Moderately differentiated tumors are the most prevalent (68.9%) type followed by Poorly differentiated (17.3%) ones and Well differentiated (13.8%) ones. This observation is concordant with most of the studies except that of Joseph et al, which observed a higher prevalence of Poorly differentiated type as given in the table below.

However, in case of Adenocarcinoma of cervix the prevalence of degree of differentiation in the present study was 75% for Moderately differentiated tumors and 25% for the Well differentiated ones. However, the studies of Joseph et al and Sarwade et al observed an equal prevalence of Well differentiated and Moderately differentiated types of adenocarcinoma of cervix.

Metastatic spread to lymph node was noted in 35.71% cases of cervical carcinomas and rest 64.29% were negative for metastases in the present study. This observation is concordant with the other studies as depicted below.

Most tumors were at Stage 3 at the time of diagnosis and Stage 4 is the least prevalent stage in the present study. The observations by various other studies are variable in the most prevalent Stage at diagnosis but all agreed that Stage 4 is the least prevalent stage at diagnosis. These observations were as depicted below.

None of the CIN cases showed positivity for Her-2/neu expression in the present study and 90.9% cases were definitely negative (0/1+) and only 9.1% were equivocal in expression. These observations are concordant with most of the other studies as depicted in the table below. However, the study of Joseph et al showed 30% cases of CIN showing equivocal expression pattern for Her-2/neu.

In cases of SCC of cervix 31.04% cases showed 3+ expression pattern for Her-2/neu followed by 2+ score in 25.86% cases, 1+ score in 22.41% cases and 0 in 20.69% cases in the present study. Other studies have differences in their observation for the same as depicted in the table below.

Similarly in cases of adenocarcinoma of cervix 66.67% cases showed 3+ expression pattern for Her-2/neu followed by 2+ score in 33.33% cases, 1+ score and 0 score was not at all observed in the present study. Other studies differ significantly in their observation for the same as depicted in the table below.

In the present study the score of Her-2/neu expression increased inversely with the degree of differentiation of the SCC cervix cases, evident from the fact that, 3+ positivity was noted in 80% of poorly differentiated SCCs, 25% of moderately differentiated ones and none of the well differentiated ones. This observation is concordant with most of the studies except that of Sarwade et al in which the rate was high for moderately differentiated ones, as depicted in the table below.

In the present study the score of Her-2/neu expression increased inversely with the degree of differentiation of the Adenocarcinoma of cervix cases and it is evident from the fact that, 3+ positivity was noted in 88.89% of moderately differentiated ones, in none of the well differentiated ones. This observation is concordant with most of the studies but that of Sarwade et al showed a different percentage, as depicted in the table below.

Most of the studies including the present study observed that Her-2/neu positivity rate increases when there is presence of lymph node metastasis except that of Sarwade et al. The observations of all the studies are depicted in the table below.

Similar to lymph node status, most of the studies including the present study observed that Her-2/neu positivity rate increases with the advanced stage of the disease at diagnosis. The observations of all the studies are depicted in the table below.

4. Limitation:

A limited sample size is one of the study's drawbacks. Premalignant lesions in particular have a tiny sample size, therefore most of the evidence is limited to studying trends and has not been confirmed statistically.

Correlation of prevalence of Histological subtypes

Histological types	Present study (%)	Gupta et al (%)	Joseph et al (%)	Sharma et al (%)	Sarvade et al (%)
Benign lesions	-	25	-	-	10
CIN	13.58	10	29.41	-	8
SCC	71.6	48	58.83	72	60
Adenocarcinoma	14.82	13	11.76	12	20
Adenosquamous-carcinoma	-	4	-	16	2

Correlation of Tumor grade of Squamous cell carcinoma

Histological grade	Present study	Gupta et al	Joseph et al	Sharma et al	Sarvade et al
Well differentiated	13.8	10.42	15	16.7	16.66
Moderately differentiated	68.9	68.75	25	44.4	53.33
Poorly differentiated	17.3	20.83	60	38.9	30

Correlation of Tumor grade of Adenocarcinoma

Tumor grade	Present study (%)	Joseph et al (%)	Sarvade et al (%)
Well differentiated	25	50	50
Moderately differentiated	75	50	50
Poorly differentiated	0	0	0

Correlation of Lymph node metastases

Lymph node status	Present study (%)	Gupta et al (%)	Joseph et al(%)	Sharma et al (%)	Sarvade et al
Positive	35.71	21.54	37.50	24	31.71
Negative	64.29	58.46	62.50	76	68.29
Not available	-	20.00	-	-	-

Correlation of Stage at diagnosis

Stage	Present study (%)	Gupta et al[15] (%)	Joseph et al(%)	Sharma et al (%)	Sarvade et al (%)
0	13.58	13.33	-	-	-
I	27.17	38.67	12.5	47.36	39.02
II	24.69	24.00	45.8	31.58	29.26
III	30.86	21.33	29.2	10.53	24.39
IV	03.70	2.67	12.5	10.53	7.31

Correlation of Her-2/neu expression in cases of CIN

Her-2/neu Expression in cases of CIN	Present study(%)	Gupta et al (%)	Joseph et al(%)	Sarvade et al (%)
0	45.45	40	30	100
1+	45.45	50	40	0
2+	9.1	10	30	0
3+	0	0	0	0

Correlation of Her-2/neu expression in cases of SCC

Her-2/neu Expression in cases of SCC	Present study(%)	Gupta et al (%)	Joseph et al(%)	Sarvade et al (%)
0	20.69	45.83	0	43.33
1+	22.41	10.42	10	26.66
2+	25.86	14.58	35	20
3+	31.04	29.17	55	10

Correlation of Her-2/neu expression in cases of Adenocarcinoma

Her-2/neu Expression in cases of Adenocarcinoma	Present study(%)	Gupta et al (%)	Joseph et al(%)	Sharma et al (%)	Sarvade et al (%)
0	0	15.38	0	0	40
1+	0	23.08	0	100	40
2+	33.33	30.77	50	0	20
3+	66.67	30.77	50	0	0

Correlation of Her-2/neu expression in different histological grades of SCC

Histological grade	Gupta et al (%)		Joseph et al (%)				Sharma et al		Sarvade et al (%)				Present study (%)			
	Present	Absent	0	1+	2+	3+	Positive	Negative	0	1+	2+	3+	0	1+	2+	3+
Well differentiated	-	100	-	33.33	66.67	-	33.3	66.7	60	40	-	-	37.5	62.5	-	-
Moderately differentiated	54.55	45.45	-	20	20	60	62.5	37.5	37.5	25	25	12.5	22.5	20	32.5	25
Poorly differentiated	80	20	-	-	33.33	66.67	71.4	28.6	44.4	22.2	22.2	11.1	-	-	20	80
P value	<0.05		0.165				0.52		0.935				0.0004			

Correlation of Her-2/neu expression in different histological grades of Adenocarcinoma

Histological grade	Joseph et al (%)				Sarvade et al (%)				Present study (%)			
	0	1+	2+	3+	0	1+	2+	3+	0	1+	2+	3+
Well differentiated	-	-	100	-	60	40	-	-	-	-	100	-
Moderately differentiated	-	-	-	100	20	40	40	-	-	-	11.11	88.89
Poorly differentiated	-	-	-	-	-	-	-	-	-	-	-	-
P value	0.0182				0.46				0.0182			

Correlation of Her-2/neu expression with Lymph node status

	Present study(%)				Sarvade et al (%)				Joseph et al (%)				Gupta et al (%)		Sharma et al (%)	
	0	1+	2+	3+	0	1+	2+	3+	0	1+	2+	3+	Present	Absent	+ve	-ve
Present	0	12	20	68	23.07	30.76	23.07	23.07	0	0	33.33	66.67	92.86	7.14	50	50
Absent	26.67	22.22	31.11	20	50	32.14	17.85	0	0	13.33	40	46.67	52.63	47.37		
Not examined	-	-	-	-	-	-	-	-	-	-	-	-	61.54	38.46	-	-
P value	0.0004				0.107				0.577				<0.05		-	

Correlation of Her-2/neu expression with Stage of the tumor at diagnosis

	Present study(%)				Sarvade et al(%)				Joseph et al(%)				Gupta et al(%)		Sharma et al(%)	
	0	1+	2+	3+	0	1+	2+	3+	0	1+	2+	3+	Present	Absent	+ve	-ve
0	45.45	45.45	9.1	0	-	-	-	-	-	-	-	-	60	40	-	-
I	40.90	36.36	18.18	4.54	56.25	37.5	6.25	0	0	0	33.33	66.67	48.28	51.72	11.11	88.89
II	10	15	45	30	36.36	27.28	36.36	0	0	9.1	45.45	45.45	72.22	27.78	66.7	33.3
III	4	8	24	64	30	30	30	10	0	14.3	42.85	42.85	87.5	12.5	50	50
IV	0	0	0	100	33.33	0	0	66.67	0	0	0	100	100	0	100	0
P value	<0.0001				0.073				0.71				<0.05		0.043	

5. Recommendation:

The data on the subject is insufficient, even for meta-analysis and pooled analysis, hence additional research with a bigger sample size is recommended.

6. Conclusions:

In the recent years there has been an outstanding advance in cervical diagnosis and management leading to earlier detection and effective treatment. This has resulted in improved quality of life with significant decline in cervical cancer deaths. Prognosis and management of cervical cancer are influenced by classic variables such as histological

type, tumor grade, lymph node status &stage of the disease at the time of diagnosis, the predictive factors include Her-2/neu status, CK-7 expression, HPV status, RAS oncogenes, P53 etc. The present study analyzed the Her-2/neu expression status with other prognostic factors in cervical carcinoma and concludes that:

- The intensity of Her-2/neu staining progressively increases with the increase in histological grade of the lesions & higher clinical stage at the time of presentation.
- Her-2/neuexpression was statistically not significant in cases of CIN.
- Her-2/neuexpression was relatively higher in cases of Adenocarcinoma of cervix as compared to SCC cervix.
- Because of the higher expression of Her-2/neuin moderately differentiated type of adenocarcinoma, Herceptin can be used as a targeted therapy in these cases.

7. Acknowledgement:

None

8. List of abbreviations:

EGFR- epidermal growth factor receptor
CIN- Cervical Intraepithelial Neoplasia
SCC- Squamous Cell Carcinoma
LSIL- low-grade intraepithelial lesion
HSIL- high-grade intraepithelial lesion

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