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Retrospective Analysis in Carcinoma Cervix with Ultrasonography and Magnetic Resonance Imaging: A Comparative Study in a Tertiary Care Hospital

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Abstract
Objectives: *To Compare the results of MRI and USG in Diagnostic accuracy, Sensitivity, Specificity in respect to diagnostic evaluation of carcinoma cervix.*
Methods: *An Institution based prospective, comparative study was done on 60 patients referred to the Dept of Radio-diagnosis, Medical College, Kolkata suspected of carcinoma cervix. After taking informed consent of the patients, USG followed by MRI were done. USG was done using Philips iU22 Ultrasound with C9-5 Transducer or C5-2 Transducer when necessary. MRI was done using GE Signa HDe 1.5T at EKO MRI Unit , Medical College, Kolkata. Definitive diagnosis was confirmed by following up the patient in either Biopsy or surgery for histopathology.*
Results: *In detection of cervical growth, sensitivity of USG (95%) was found to be slightly better than MRI (93.3%).*
In comparison of USG with histopathology in detection of stromal invasion of >2/3RD sensitivity of USG was 100%, specificity of USG – 72.2%, positive predictive value- 78.26% and negative predictive value – 100%. ***p value <0.0001, statistically significant.***
In comparison of MRI with histopathology in detection of stromal invasion of >2/3RD sensitivity of MRI was 94.4%, specificity of MRI – 88.8%, positive predictive value- 89.47% and negative predictive value – 94.12%. ***p value - <0.0001, statistically significant.***
In comparison of USG with histopathology in detection of parametrical invasion sensitivity of USG was 62.5%, specificity of USG – 85.7%, positive predictive value- 55.5%, negative predictive value – 88.89%. ***p value - 0.0651, statistically not significant.***
In comparison of MRI with histipathology in detection of parametrial invasion sensitivity of MRI was 50%, specificity of MRI – 85.7%, positive predictive value- 50% and negative predictive value – 85.71%. ***p value - 0.371, statistically not significant.***
Conclusion: *Although Ultrasound and MRI both missed smaller lesions, they showed more accuracy compared to clinical evaluation for detection of stromal & parametrial invasion, assessment of accurate tumor size and extension. Whereas, clinical evaluation gives better result for vaginal involvement.*
For detection of stromal invasion >2/3rd, both USG & MRI had high sensitivity and specificity; however, USG had 100% sensitivity and negative predictive value.
A clinical staging method can pick up smaller lesions and vaginal invasion more accurately, while MRI, which is significantly costly but a non invasive non ionizing imaging modality, if implemented as part of carcinoma cervix diagnostic work up can assess stromal and parametrial invasion, adjacent organ involvement more accurately and in many cases avoiding unnecessary invasive procedures which decide the stage and further management. Thus it is recommended that MRI should be included in the routine staging of all the advanced cases of carcinoma cervix.
USG due to it's relatively low cost, widespread availability and the rapidity of the procedure with recent advances in technology and equipments have similar accuracy to MRI and higher accuracy to clinical staging in assessing stromal, parametrial and adjacent organ involvement.
Thus, in the hands of an experienced examiner it may be considered as the first-line diagnostic method and it is recommended that Ultrasound should be included in the routine staging of all cases of carcinoma cervix.

Keywords: *Carcinoma cervix, Ultrasonography, MRI, FIGO staging, stromal invasion, parametrial invasion, comparative study.*

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I. Introduction

Although the overall mortality of patients with carcinoma of the uterine cervix has decreased over the years on account of the widespread availability of effective screening programs, cervical cancer ranks third worldwide among gynecological malignancies, with an age standardized incidence of 8.9 per 100 000 women/year, and an estimated 9710 new cases per year in the United States. Overall, the 5 year survival rate has been reported to be 73%, but the prognosis for the subgroup with locally advanced cervical cancer still remains unsatisfactory[1]. Cervical cancer is still the commonest cancer causing death among women in developing countries. In India, carcinoma of cervix contributes to approximately 6-29% of all cancers in women.

Assessment of the extent of the disease is crucial in planning the optimal treatment strategy. The International Federation of Gynecology and Obstetrics (FIGO) recommends a clinical staging system for cervical carcinoma based on findings from physical examination performed under anesthesia, colposcopy with biopsies of the lesion, chest radiography, cystoscopy, sigmoidoscopy, intravenous excretory urography and barium enema studies[2]. When comparing the FIGO staging with the surgical and pathological data, there is an underestimation of the extent of the disease in 17–32% of cases classed as stage IB, rising to 67% in stages II–IV of the disease [3-5]. The use of sophisticated radiological examinations, such as computed tomography (CT) and magnetic resonance imaging (MRI), has entered into routine practice, even if these methods are not regarded as obligatory in the assessment of clinical staging according to FIGO. The issues of costs, availability and dedicated radiological training call for the evaluation of imaging approaches other than CT and MRI. Given the great advances in ultrasound technology and equipment documented in recent decades, and considering its low cost and wide availability, it is reasonable to consider ultrasound as a potential diagnostic tool for cervical cancer staging. The FIGO (INTERNATIONAL FEDERATION OF GYNECOLOGISTS and OBSTETRICIANS) staging of invasive cervical cancer is solely clinical and based on the findings on Chest Radiography, Intravenous Urogram (IVU) and Barium enema. However it has several limitations. Estimation of tumor size, stromal invasion and spread may not be always accurate on clinical examination and lymph node status assessment is not included. Tumor size and Lymph node status are important prognostic markers both of which can be accurately assessed by Ultrasound and MRI. Tumor extension into vagina and parametrium can be identified by USG and MRI. Evidence of urinary obstruction (hydro-ureteronephrosis) on IVU is classified as stage IIIB, which can easily be evaluated in transabdominal USG. Imaging aids in choosing the most appropriate treatment options without altering the clinical stage. My study is to assess, correlate and compare the results of USG and MRI in diagnostic accuracy, sensitivity and specificity of carcinoma cervix.

Cancer of the cervix is a largely preventable disease that is characterized by a long lead time. The disease is potentially curable if identified before progression into invasive carcinoma. However, invasive cervical carcinoma remains a disease of significant morbidity and mortality.

Early exposure to coitus, sexual promiscuity, high parity, low socio- economic status, sexually transmitted HPV (16, 18, 6, 11) infection are the risk factors for development of cervical carcinoma.

The prognosis depends on clinical stage, tumor size, histologic grade and lymph node status. The clinical stage is determined by FIGO staging which includes the findings on hysteroscopy, cystoscopy, proctoscopy, endocervical curettage, IVP, barium enama and chest radiography. However, there are significant inaccuracies in clinical staging. Without cross-sectional imaging, there is poor evaluation of deep pelvic invasion. Moreover, tumor size and nodal metastasis- the two most important prognostic markers are not assessed.

MRI due to its excellent soft tissue contrast resolution which exceeds that of CT scan, has become a valuable non-invasive, non-ionizing imaging modality in pre-treatment evaluation of cancer cervix. However, there is a significant difference in the cost and availability of MRI and ULTRASONOGRAPHY. So the cost benefit ratio of an expensive modality like MRI and its less availability in rural population warrants a comparison and correlation of Ultrasonographic findings and their imaging characteristics with MRI findings which form the basis of this study.

II. Materials and Method

An Institution based prospective, comparative study was done on 60 patients referred to the Dept of Radio-diagnosis, Medical College, Kolkata suspected of carcinoma cervix. After taking informed consent of the patients, USG followed by MRI were done. USG was done using Philips iU22 Ultrasound with C9-5 Transducer or C5-2 Transducer when necessary. MRI was done using GE Signa HDe 1.5T at EKO MRI Unit , Medical College, Kolkata. Definitive diagnosis was confirmed by following up the patient in either Biopsy or surgery for histopathology. The study period was between Jan 17 to Aug 18.

The patients who on clinical examination were suspected or diagnosed to have carcinoma cervix and Patients with incidentally detected cancer cervix on Ultrasonography were included.

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for

numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value is below the threshold chosen for statistical significance usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis.
p-value ≤ 0.05 was considered for statistically significant.

III. Results

Table1: Distribution of Age in Years

Age in Years	Frequency	Percent
≤30	1	1.7%
31-40	18	30.0%
41-50	24	40.0%
51-60	16	26.7%
61-70	1	1.7%
Total	60	100.0%

1(1.7%) patient was in ≤30 years age group, 18(30.0%) patients were in 31-40 years age group, 24(40.0%) patients were in 41-50 years age group, 16(26.7%) patients were in 51-60 years age group and 1(1.7%) patient was in 61-70 years age group.

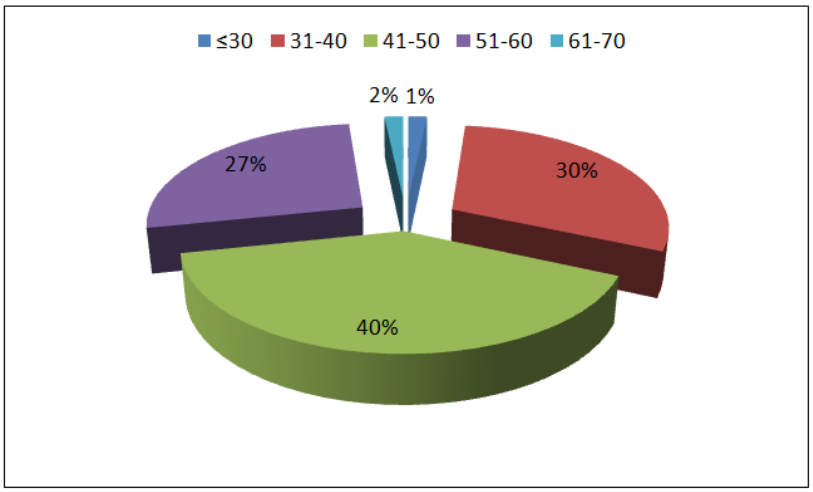
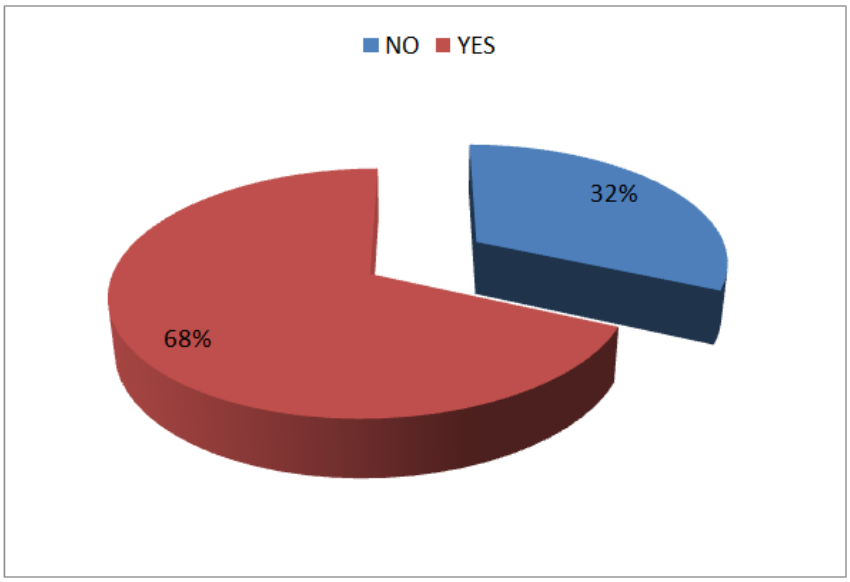


Table 2: Distribution of visible/palpable growth

VISIBLE/PALPABLE GROWTH	Frequency	Percent
NO	19	31.7%
YES	41	68.3%
Total	60	100.0%

41(68.3%) patients had visible/palpable growth.

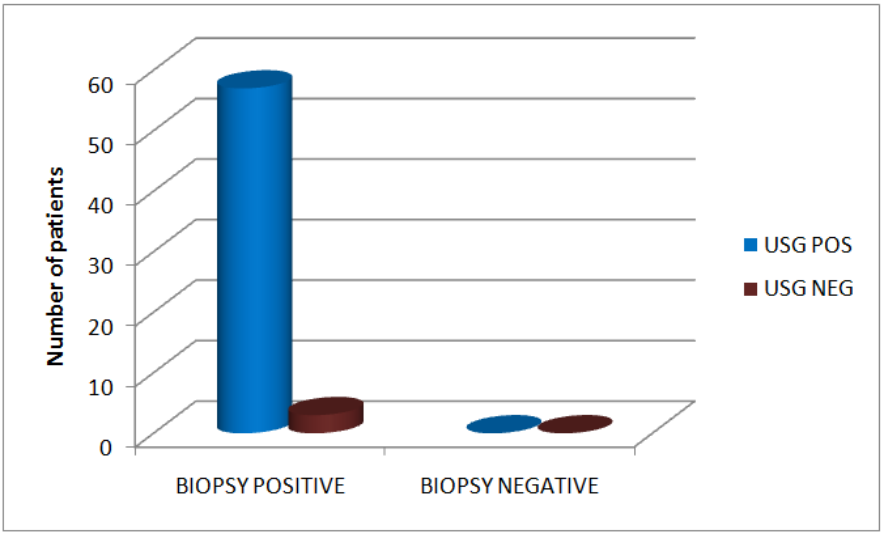


Comparison Of Usg With Histipathology In Detection Of Cervical Mass

	BIOPSY POSITIVE	BIOPSY NEGATIVE	TOTAL
USG POS	57	0	57
USG NEG	3	0	3
TOTAL	60	0	60

Out of the 60 histologically positive cases of carcinoma cervix in our study, USG showed the presence of growth in 57 cases& MRI in 56 cases. However, USG failed to detect cervical growth in 3 cases & MRI in 4 cases.

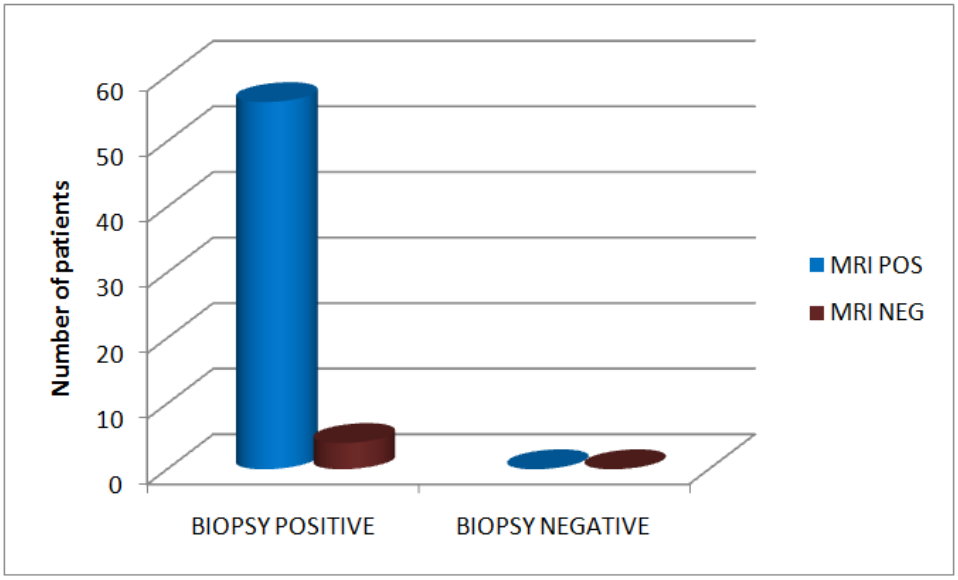
Sensitivity USG - 95%
p<0.0001, Statistically significant



Comparison Of Mri With Histipathology In Detection Of Cervical Mass

	BIOPSY POSITIVE	BIOPSY NEGATIVE	TOTAL
MRI POS	56	0	56
MRI NEG	4	0	4
TOTAL	60	0	60

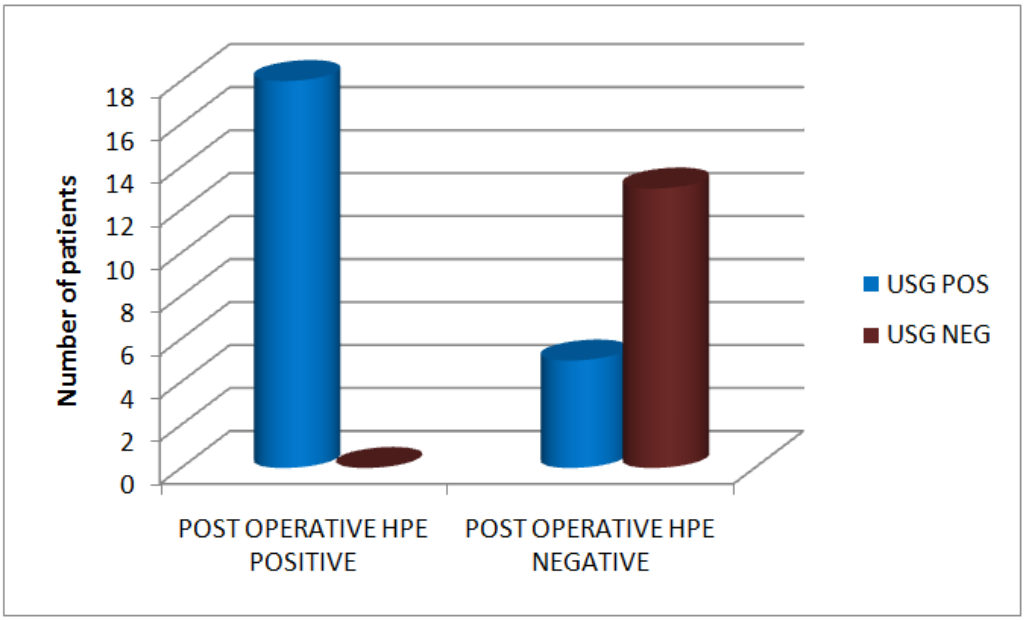
Sensitivity MRI – 93.3 %
p<0.0001, Statistically significant



Comparison of USG With Histipathology In Detection Of Stromal Invasion Of >2/3rd

	POST OPERATIVE HPE POSITIVE	POST OPERATIVE HPE NEGATIVE	TOTAL
USG POS	18	5	23
USG NEG	0	13	13
TOTAL	18	18	36

SENSITIVITY OF USG – 100%
SPECIFICITY OF USG – 72.2%
POSITIVE PREDICTIVE VALUE- 78.26%
NEGATIVE PREDICTIVE VALUE – 100%
P VALUE - <0.0001, statistically significant



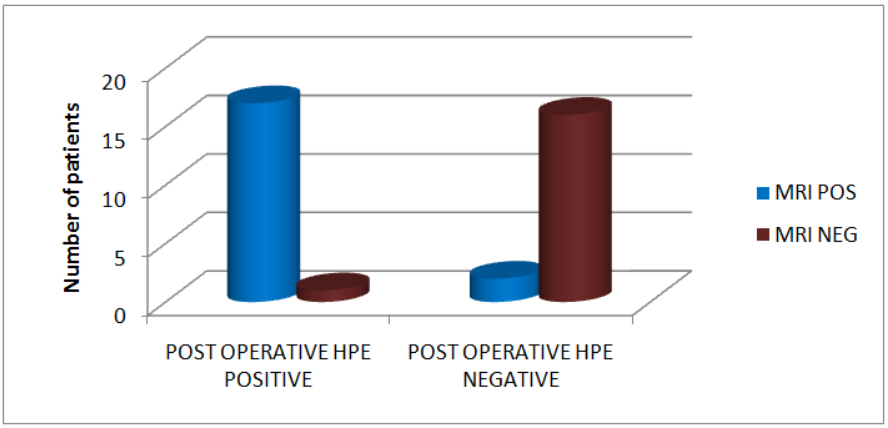
Comparison of Mri With Histipathology In Detection Of Stromal Invasion Of >2/3rd

	POST OPERATIVE HPE POSITIVE	POST OPERATIVE HPE NEGATIVE	TOTAL
MRI POS	17	2	19
MRI NEG	1	16	17
TOTAL	18	18	36

SENSITIVITY OF MRI – 94.4%

SPECIFICITY OF MRI – 88.8%
POSITIVE PREDICTIVE VALUE- 89.47%
NEGATIVE PREDICTIVE VALUE – 94.12%
P VALUE - <0.0001, statistically significant

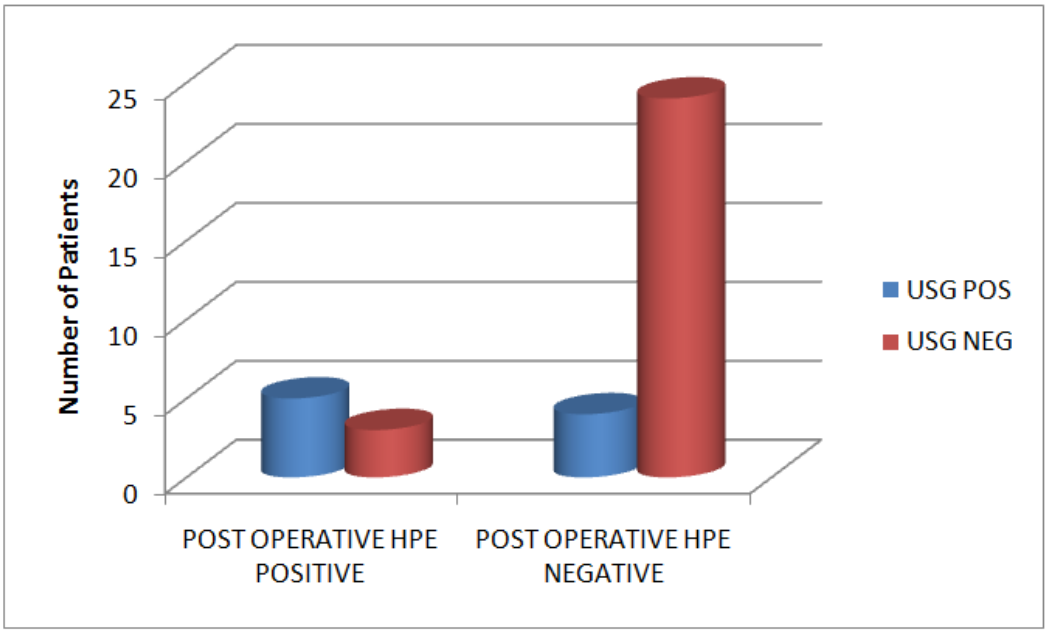
Out of the 60 cases evaluated in our study, post operative histopathology data were available for only 36 cases. Of these 36 cases, 18 cases showed cervical stromal involvement of >2/3rd and 18 cases showed no more than 2/3rd involvement on histopathology. Of these 18 cases of stromal invasion of >2/3rd by histopathology, USG showed stromal involvement of >2/3rdin all the 18 cases and MRI in 17 cases. USG gave false positive result in 5 cases and MRI in 2 cases.



Comparison Of Usg With Histipathology In Detection Of Parametrial Invasion

	POST OPERATIVE HPE POSITIVE	POST OPERATIVE HPE NEGATIVE	TOTAL
USG POS	5	4	9
USG NEG	3	24	27
TOTAL	8	28	36

SENSITIVITY OF USG – 62.5%
SPECIFICITY OF USG – 85.7%
POSITIVE PREDICTIVE VALUE- 55.5%
NEGATIVE PREDICTIVE VALUE – 88.89%
P VALUE - 0.0651, statistically not significant



Comparison of MRI With Histipathology In Detection Of Parametrial Invasion

	POST OPERATIVE HPE POSITIVE	POST OPERATIVE HPE NEGATIVE	TOTAL
MRI POS	4	4	8
MRI NEG	4	24	28
TOTAL	8	28	36

SENSITIVITY OF MRI – 50%
SPECIFICITY OF MRI – 85.7%
POSITIVE PREDICTIVE VALUE- 50%
NEGATIVE PREDICTIVE VALUE – 85.71%
P VALUE - 0.371, statistically not significant

Out of the 60 cases evaluated in our study, post operative histopathology data were available for only 36 cases.Of these 36 cases, 8 cases showed parametrial invasion on histopathology. Of these 8 cases, USG showed parametrial invasion in 5 cases and MRI in 4 cases. Rest of the 3 cases in USG and 4 cases in MRI appeared negative for parametrial invasion, which were histopathologically positive. USG & MRI both gave false positive result in 4 cases for parametrial invasion which were histopathologically negative. 24 cases showed no parametrial invasion in USG & MRI which in histopathology also showed no invasion.

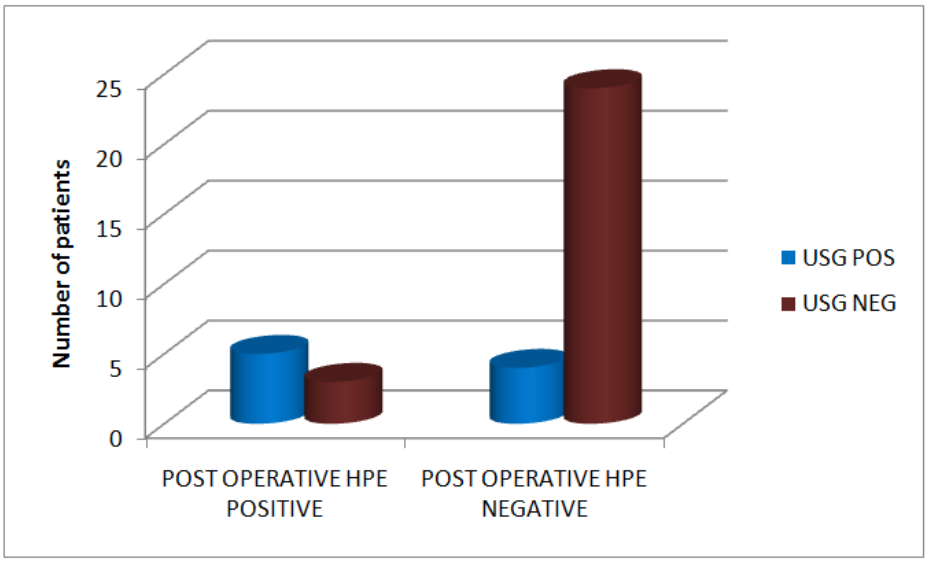


Table 3: Distribution Based On Vaginal Involvement on Usg and Mri

VAGINAL INVOLVEMENT	USG CASES	PERCENTAGE	MRI CASES	PERCENTAGE	CLINICAL	PERCENTAGE
NO VAGINAL INVOLVEMENT	33	55%	33	55%	30	50%
UPPER 2/3rd	17	28.3%	17	28.3%	20	33.3%
LOWER 1/3rd	10	16.7%	10	16.7%	10	16.7%
TOTAL	60	100%	60	100%	60	100%

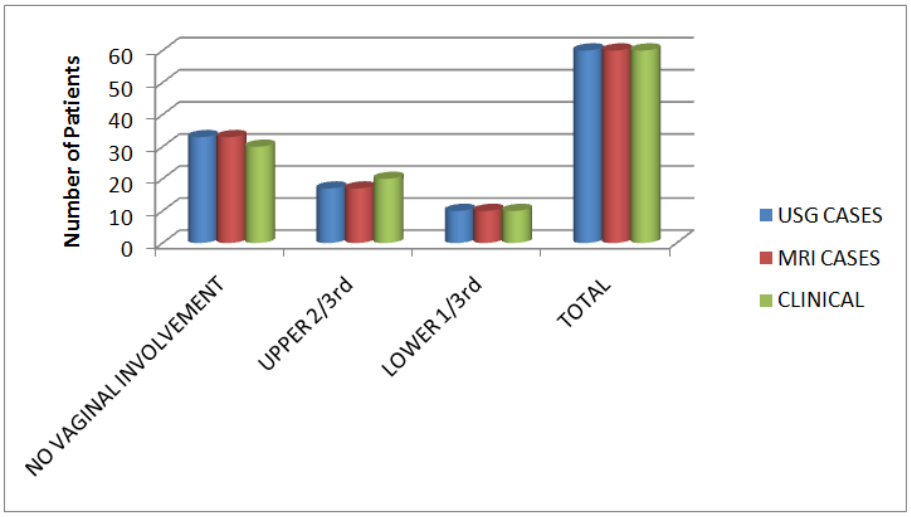


Table 4: Results of Parameters for Clinical Staging

FINDINGS	NO. OF CASES
LESIONS CLINICALLY VISIBLE	58
UPPER 2/3rd VAGINA	20
LOWER 1/3rd VAGINA	10
PARAMETRIAL INVOLVEMENT	17
PELVIC SIDE WALL INVOLVEMENT	12
UB/RECTUM INVOLVEMENT	5
DISTANT METASTASIS	2

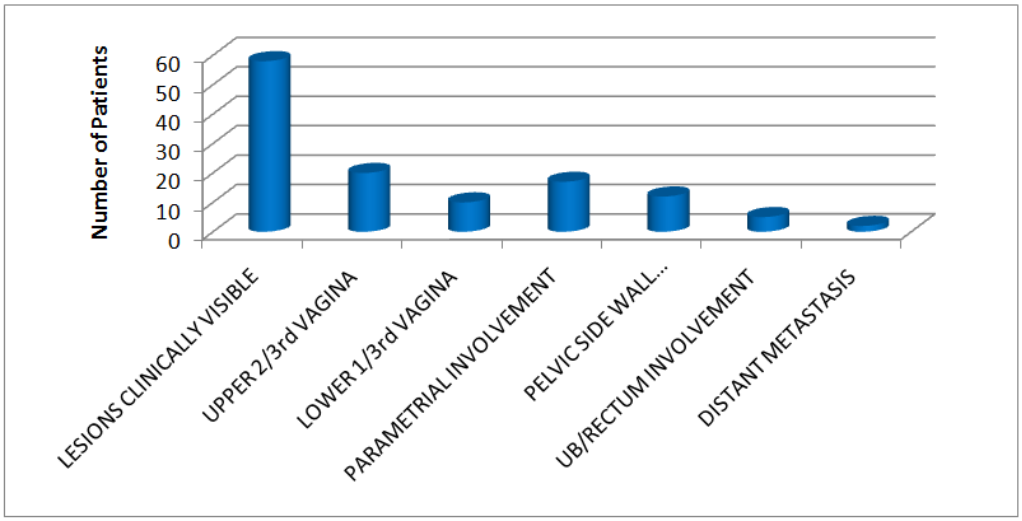


Table 5: Distribution of final USG staging

FINAL USG STAGING	**Frequency**	**Percent**
IB	15	25.0%
IIA	9	15.0%
IIB	16	26.7%
IIIA	7	11.7%
IIIB	4	6.7%
IVA	4	6.7%
IVB	2	3.3%
N	3	5.0%
Total	60	100.0%

According to final USG staging, 15(25.0%) patients had IB, 9(15.0%) patients had IIA, 16(26.7%) patients had IIB, 7(11.7%) patients had IIIA, 4(6.7%) patients had IIB, 4(6.7%) patients had IV A, 2(3.3%) patients had IVB and 3(5.0%) patients had N.

Distribution of final USG staging

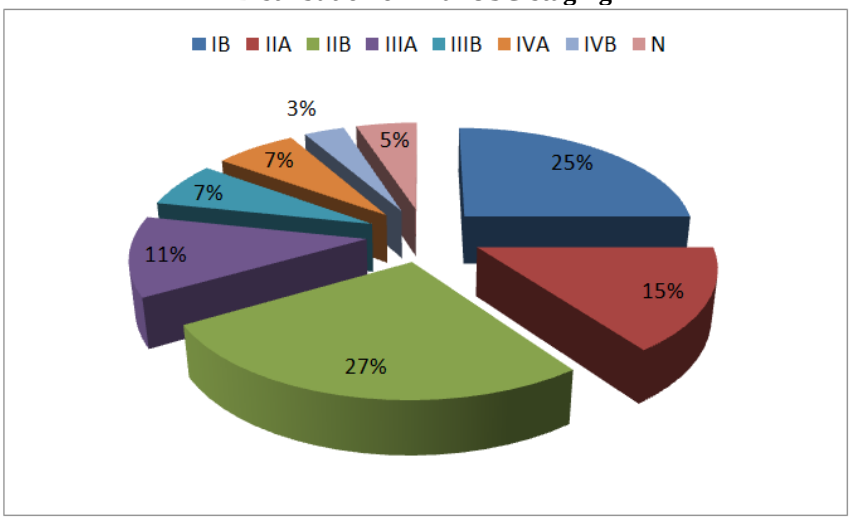
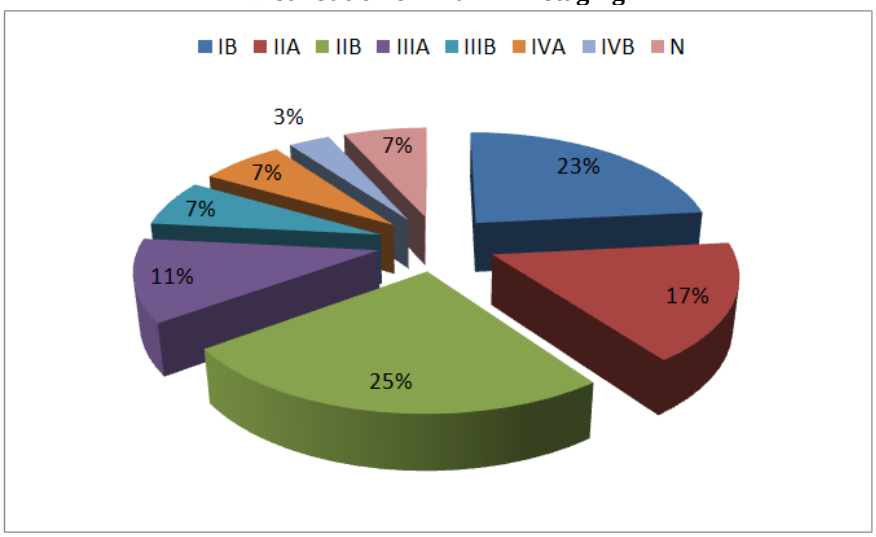


Table 6: Distribution of Final MRI Staging

FINAL MRI STAGING	Frequency	Percent
IB	14	23.3%
IIA	10	16.7%
IIB	15	25.0%
IIIA	7	11.7%
IIIB	4	6.7%
IVA	4	6.7%
IVB	2	3.3%
N	4	6.7%
Total	60	100.0%

According to final MRI staging, 14(23.3%) patients had IB, 10(16.7%) patients had IIA, 15(25.0%) patients had IIB, 7(11.7%) patients had IIIA, 4(6.7%) patients had IIIB, 4(6.7%) patients had IVA, 2(3.3%) patients had IVB and 4(6.7%) patients had N.

Distribution of final MRI staging



IV. Discussion

In our study of carcinoma Cervix in 60 patients, We compared the two diagnostic modalities- USG (TVS/TAS) and MRI with histopathological findings as the gold standard.

Out of the 60 histologically positive cases of ca cervix in our study, USG showed the presence of growth in 57 cases& MRI in 56 cases. However, USG failed to detect cervical growth in 3 cases & MRI in 4 cases. Sensitivity USG was 95%. P value <0.0001, Statistically significant. Sensitivity MRI – 93.3 % & p value <0.0001, Statistically significant.

Out of the 60 cases evaluated in our study, post operative histopathology data were available for only 36 cases. Of these 36 cases, 18 cases showed cervical stromal involvement of >2/3rd and 18 cases showed no more than 2/3rd involvement on histopathology. Of these 18 cases of stromal invasion of >2/3rd by histopathology, USG showed stromal involvement of >2/3rdin all the 18 cases and MRI in 17 cases. USG gave false positive result in 5 cases and MRI in 2 cases.

In comparison of USG with histopathology in detection of stromal invasion of >2/3RD sensitivity of USG was 100%, specificity of USG – 72.2%, positive predictive value-78.26% and negative predictive value – 100%. **p value <0.0001, statistically significant.**

In comparison of MRI with histopathology in detection of stromal invasion of >2/3RD sensitivity of MRI was 94.4%, specificity of MRI – 88.8%, positive predictive value- 89.47% and negative predictive value – 94.12%. **p value - <0.0001, statistically significant.**

Out of the available post operative histopathology data of 36 cases in our study, 8 cases showed parametrial invasion on histopathology. Of these 8 cases, USG showed parametrial invasion in 5 cases and MRI in 4 cases. Rest of the 3 cases in USG and 4 cases in MRI appeared negative for parametrial invasion, which were histopathologically positive. USG &

MRI both gave false positive result in 4 cases for parametrial invasion which were histopathologically negative. 24 cases showed no parametrial invasion in USG & MRI which in histopathology also showed no invasion.

In comparison of USG with histopathology in detection of parametrical invasion sensitivity of USG was 62.5%, specificity of USG – 85.7%, positive predictive value- 55.5%, negativepredictive value – 88.89%. **p value - 0.0651, statistically not significant.**

In comparison of MRI with histipathology in detection of parametrial invasion sensitivity of MRI was 50%, specificity of MRI – 85.7%, positive predictive value- 50% and negative predictive value – 85.71%. **p value - 0.371, statistically not significant.**

Of the 36 post operative cases, 8 cases showed parametrial invasion on histopathology. Of these 8 cases, clinical evaluation showed parametrial invasion in 5 cases. Rest of the 3 cases appeared negative for parametrial invasion, which were histopathologically positive. Clinical evaluation gave false positive result in 2 cases for parametrial invasion which were histopathologically negative. 26 cases showed no parametrial invasion clinically which in histopathology also showed no invasion.

Lymph node enlargement (in the short axis > 10mm approx.) is an additional finding which can be detected by both Ultrasound and MRI, which is not evaluated clinically and therefore, not included in the FIGO Staging system (2009). Initial knowledge about the lymph node status can help plan appropriate management guideline and response assessment later on. However, lymphadenopathy detected on USG and MRI can not reliably differentiate between metastatic lymph nodes or reactive inflammatory lymphadnopathy.

Critical aspects of ultrasound examination is the operator's practical skill when carrying out the examination and expertise in interpreting the images obtained. On the other hand, even MRI images need to be interpreted, and this interpretation is liable to as much subjectivity as the interpretation of ultrasound images. Disadvantages of MRI are its cost and the fact that a dynamic examination is not possible. Moreover, it is also time consuming and not universally available. Some might suggest that three-dimensional (3D) ultrasound would overcome the problem with the need for ultrasound operator skill, because it allows off-line analysis of volumes [6]. However, the acquisition of an ultrasound volume and the interpretation of 3D images require at least as much skill as the acquisition and interpretation of two-dimensional images.

V. Conclusion

Although Ultrasound and MRI both missed smaller lesions, they showed more accuracy compared to clinical evaluation for detection of stromal & parametrial invasion, assessment of accurate tumor size and extension. Whereas, clinical evaluation gives better result for vaginal involvement.

For detection of stromal invasion >2/3rd, both USG & MRI had high sensitivity and specificity; however, USG had 100% sensitivity and negative predictive value.

A clinical staging method can pick up smaller lesions and vaginal invasion more accurately, while MRI, which is significantly costly but a non invasive non ionizing imaging modality, if implemented as part of carcinoma cervix diagnostic work up can assess stromal and parametrial invasion, adjacent organ involvement

more accurately and in many cases avoiding unnecessary invasive procedures which decide the stage and further management. Thus it is recommended that MRI should be included in the routine staging of all the advanced cases of carcinoma cervix.

USG due to it's relatively low cost, widespread availability and the rapidity of the procedure with recent advances in technology and equipments have similar accuracy to MRI and higher accuracy to clinical staging in assessing stromal, parametrial and adjacent organ involvement.

Thus, in the hands of an experienced examiner it may be considered as the first-line diagnostic method and it is recommended that Ultrasound should be included in the routine staging of all cases of carcinoma cervix.

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