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Role Of MR Imaging On Diagnosis, Staging And Follow Up Of Patients With Carcinoma Cervix

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Abstract

Background :Cervical cancer is the fourth most common cancer in women worldwide and the most common gynaecological malignancy. The FIGO staging system is the most commonly utilised classification system for cervical cancer worldwide. Prior to the most recent update in the FIGO staging in 2018, the staging was dependent upon clinical assessment alone. Concordance between the surgical and clinical FIGO staging decreases rapidly as the tumour becomes more advanced. MRI now plays a central role in patients diagnosed with cervical cancer and enables accurate staging, which is essential to determining the most appropriate treatment. MRI is the best imaging option for the assessment of tumour size, location, and parametrial and sidewall invasion. Notably, the presence of parametrial invasion precludes surgical options, and the patient will be triaged to chemoradiotherapy. As imaging is intrinsic to the new 2018 FIGO staging system, nodal metastases have been included within the classification as stage IIIC disease. The presence of lymph node metastases within the pelvis or abdomen is associated with a poorer prognosis, which previously could not be included in the staging classification as these could not be reliably detected on clinical examination.

Aim Of The Study: To evaluate the efficacy of MRI in assessment of important prognostic factors in carcinoma cervix like tumor size, involvement of parametrium, involvement of pelvic side wall, involvement of adjacent organs and the nodal status and how it alters the plan of management.To study the role of MRI in detecting the recurrence of carcinoma cervix in patients treated with radiotherapy.

Methods: The study was conducted in the year 2022,in Department of Radiodiagnosis, Yashoda Hospitals**,** Hyderabad, Telangana, India. around 70 patients who were histopathologically proven cases of carcinoma cervix and referred for MRI pelvis to the Department of Radio diagnosis were included in the study. Histopathogically diagnosed cases of carcinoma cervix who were referred to the Department of Radio diagnosis were included. In this study, two groups of patients were included– newly diagnosed and post treatment cases. After obtaining permission from the institutional medical research ethics committee and taking informed consent from the patients, they were subjected to MRI pelvis using a 1.5 – Tesla system. Different MRI sequences like TRUFI coronal, axial and sagittal T2WTSE, axial and sagittal T1WTSE, STIR axial, DWI – MRI with ADC and contrast enhanced oblique axial, coronal and sagittal FST1 WTSE were used. The contrast gadolinium DTPA was given at a dose of 0.1 mmol / kg at a rate of 1 ml / second.

Results: The most common histopathological type was squamous cell carcinoma which was seen in 92% of the newly diagnosed cases and the remaining 8% is constituted by adenocarcinoma. Squamous cell carcinoma is the most common histological subtype in post treatment cases also (in 41 patients). Adenocarcinoma was seen in 3 patients. 9 patients were post hysterectomy cases. Among them, 4 cases underwent hysterectomy for benign

causes and postoperatively, histopathologic reports revealed carcinoma cervix. None of them had preoperative MRI. One patient underwent surgery for CIN III and was proven to be stage IIA postoperatively. One patient was diagnosed with early stage disease and underwent hysterectomy and was staged postoperatively as IIB. MRI also showed parametrial invasion at the end of 6 months of radiotherapy. This patient had no preoperative MRI. One patient had carcinoma ovary. In our study, among the 26 newly diagnosed cases (biopsy proven), T2 W, DWI and contrast enhanced imaging showed lesions in 24, 25 and 23 cases respectively. One case did not show T2 hyperintensity or contrast enhancement. However, the cervix appeared bulky with heterogenous signal. One case did not undergo contrast study and showed normal T2 signal intensity but showed diffusion restriction. In another case the tumour showed poor enhancement but T2 hyperintense signal and diffusion restriction were noted. Thus, DWI- MRI was able to diagnose 96% of cases and T2 W and contrast images detected 92% cases. A combination of T2 W and DWI detected lesion in 24 cases. Whereas the one case showing only diffusion restriction needed confirmation with biopsy. A combination of T2 W and contrast imaging diagnosed 23 cases while missing 2 cases. The accuracy, sensitivity, positive and negative predictive values of MRI in newly diagnosed cases are 88.19%, 88%, 92.59% and 95.65% respectively. In the post treatment cases, primary group of nodes was involved in 5 patients and secondary group in 4 patients. Among the patients with secondary nodes involvement, inguinal nodes were involved in 2 patients, paraaortic nodes in one patient and common iliac nodes in 2 patients. In our study, hydrometra was present in 29 cases (41%). Among these, 14 cases were newly diagnosed and 15 patients were post treatment cases. Among the 15 post treatment cases, 10 patients had demonstrable mass lesion on MRI.

Conculsion : MRI is integral to the management of cervical cancer, having been formally incorporated into the updated 2018 FIGO staging system. MRI allows the accurate assessment of tumour size, parametrial involvement, and lymph node involvement, which are crucial for triaging patients into those that will be eligible for primary surgery or chemoradiotherapy. MRI has applications for radiotherapy planning and image-guided adaptive brachytherapy. It also has a role in evaluating treatment response and detecting tumour recurrence and possible treatment complications.

Keywords: Gynaecological Malignancy; Cervical Malignancy; Figo Staging; MRI

Introduction

Cervical cancer is the fourth most common gynaecological cancer worldwide, with a peak incidence between 25 and 40 years [1]. GLOBOCAN 2020 estimated that, worldwide, there were approximately 604 000 new cases of cervical cancer and 342 000 deaths due to the disease annually. Most new cases (approximately 90%) occur in low- and middle-income countries, where cervical cancer represents the third most common cancer in women.

One of the main risk factors is long-term or persistent infection with human papillomavirus (HPV). Over 70% of newly diagnosed cervical cancers are caused by either the HPV 16 or 18 subtypes. A further 19% of cervical cancers are caused by the HPV types 31, 33, 45, 52, or 58 [2]. HPV is a ubiquitous sexually transmitted infection with a prevalence of 11.7% globally, with a geographic distribution ranging from 2% to 42% [3]. The majority of HPV infections are cleared by women in two years, and only 10% cause a persistent infection.This knowledge of HPV epidemiology has led the World Health Organisation (WHO) to call for a worldwide HPV eradication program [4]. The WHO global strategy proposes that a 90–70–90 target be met by 2030 for countries to be on the path towards eliminating cervical cancer. This target aims for 90% of girls to be fully vaccinated with the HPV vaccine by 15 years old, 70% of women to be screened with a high-performance test by 35 years of age and again by 45 years of age, and 90% of women affected by a cervical disease (precancer and invasive cancer) to receive treatment [5].Cervical cancers are differentiated into different histological types, with the commonest being squamous cell carcinomas, constituting approximately 70-80% of cervical cancers. The glandular histological subtypes include

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adenocarcinomas, which account for a further approximately 25% of cervical cancers and are typically associated with a poorer prognosis [6]. Rarer subtypes include carcinosarcoma, adenosquamous carcinoma, and adenosarcoma. MR imaging of cervix has evolved over the past two decades as the most useful imaging. It is not only useful for preoperative staging but it also helps in identification of recurrent / residual tumors in treated patients.Carcinoma cervix is the most common gynaecological cancer in India and the second most common cancer worldwide. It predominantly affects multiparous women and it is transmitted by human papilloma virus infection. 2, 88,000 deaths occur annually worldwide due to carcinoma cervix. Incidence of carcinoma cervix rises from 30 – 34 years and peaks at 50-55 years.[7] The prevalence of cervical carcinoma has increased in recent years due to early screening programs.The screening programs prompt the patients to undergo further evaluation. MR imaging proves to be the next best level of modality in cervical carcinoma. MRI accurately stages the carcinoma which is better than clinical staging.[8]

Methods: The study was conducted in the year 2022,in Department of Radiodiagnosis, Yashoda Hospitals, Hyderabad, Telangana, India. around 70 patients who were histopathologically proven cases of carcinoma cervix and referred for MRI pelvis to the Department of Radio diagnosis were included in the study. Histopathogically diagnosed cases of carcinoma cervix who were referred to the Department of Radio diagnosis were included. In this study, two groups of patients were included– newly diagnosed and post treatment cases. After obtaining permission from the institutional medical research ethics committee and taking informed consent from the patients, they were subjected to MRI pelvis using a 1.5 – Tesla system. Different MRI sequences like TRUFI coronal, axial and sagittal T2WTSE, axial and sagittal T1WTSE, STIR axial, DWI – MRI with ADC and contrast enhanced oblique axial, coronal and sagittal FST1 WTSE were used. The contrast gadolinium DTPA was given at a dose of 0.1 mmol / kg at a rate of 1 ml / second. Inclusion Criteria:Carcinoma cervix patients who were referred to our department for MR imaging both newly diagnosed and those who were on post treatment follow up.Exclusion Criteria:Patients with cardiac pacemakers, new implants, clips within the body and other contraindications of MR imaging like claustrophobia were excluded.

Results

The age group of patients under study is a wide range from 35 years to 73 years. In general, majority of the patients belonged to the age group of 41- 50 years (38% of study population) followed by 51-60 years (31% of the population). 6 patients belonged to less than 40 years of age. Among the new cases diagnosed, majority of them belonged to age more than 60. But, among the recurrent cases, the common age group is 41- 50 years. Common histopathological typewas squamous cell carcinoma which was seen in 92% of the newly diagnosed cases and the remaining 8% is constituted by adenocarcinoma. Squamous cell carcinoma is the most common histological subtype in post treatment cases also (in 41 patients). Adenocarcinoma was seen in 3 patients. 9 patients were post hysterectomy cases. Among them, 4 cases underwent hysterectomy for benign causes and postoperatively, histopathologic reports revealed carcinoma cervix. None of them had preoperative MRI. One patient underwent surgery for CIN III and was proven to be stage IIA postoperatively. One patient was diagnosed with early stage disease and underwent hysterectomy and was staged postoperatively as IIB. MRI also showed parametrial invasion at the end of 6 months of radiotherapy. This patient had no preoperative MRI. One patient had carcinoma ovary coexisting with carcinoma cervix. Post surgically, a carcinoma of cervix stage IB was diagnosed. MRI also showed mass lesion involving cervix in this case. Two patients underwent hysterectomy before 4 years and now are diagnosed with vault recurrence. Among these two, only one patient clinically showed mass and the other was diagnosed with MRI.Radiotherapy was given for 39 patients totally and most of them (13 patients, 33%) were symptomatic and referred for MRI during the period of 1- 5 years followed by less than 6 months and during the period of 6- 12 months. Clinical vs MRI staging in new cases.The accuracy, sensitivity, positive and negative predictive values of MRI in newly diagnosed cases are 88.19%, 88%, 92.59% and 95.65% respectively. For all the newly diagnosed cases staged with FIGO system using clinical examination and MRI, correlation was the best for stage II B disease and higher staging was given with

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MRI to clinical stage III disease. MRI staging correlated with clinical staging in 31% of new cases and there was up staging with MRI for 42% of cases and down staging for 27% of cases. In our study, significantly, 8 cases which were diagnosed as stage IIIB clinically were found to be stage IV A with MRI. Two cases of clinically staged IIA were actually found to have bladder invasion on MRI and hence staged as IV A. Cystoscopy showed bladder invasion in 4 cases. However, on MRI, 9 cases were diagnosed. One patient had both carcinoma of rectum and cervix. Apart from this one more case was identified with rectal infiltration in sigmoidoscopy. However, MRI showed 3 cases with rectal infiltration. In our study, primary group of lymph nodes (parametrial, obturator, external and internal iliac nodes) was involved in 6 patients among the newly diagnosed. Secondary group of lymph nodes was involved in 3 patients. One patient showed paraaortic node and the other two showed common iliac nodes. In our study, among the 26 newly diagnosed cases (biopsy proven), T2 W, DWI and contrast enhanced imaging showed lesions in 24, 25 and 23 cases respectively. One case did not show T2 hyperintensity or contrast enhancement. However, the cervix appeared bulky with heterogenous signal. One case did not undergo contrast study and showed normal T2 signal intensity but showed diffusion restriction. In another case the tumour showed poor enhancement but T2 hyperintense signal and diffusion restriction were noted. Thus, DWI- MRI was able to diagnose 96% of cases and T2 W and contrast images detected 92% cases. A combination of T2 W and DWI detected lesion in 24 cases. Whereas the one case showing only diffusion restriction needed confirmation with biopsy. A combination of T2 W and contrast imaging diagnosed 23 cases while missing 2 cases. The accuracy, sensitivity, positive and negative predictive values of MRI in newly diagnosed cases are 88.19%, 88%, 92.59% and 95.65% respectively.In our study considering the 44 post treatment cases, clinically mass was suspected in 30 patients (68% cases). But MRI showed the presence of mass lesion in only 16 patients. Eight patients were referred for routine follow up and they had no clinically identifiable mass lesion. Among these 8 patients, two showed lesion on MRI. In another 6 patients, cervix couldn't be clinically examined due to practical difficulties. Among these 6 patients, four showed presence of mass lesion. The accuracy, sensitivity, specificity, positive and negative predictive values of MRI in recurrent cases are 57.89%, 88.89%, 30%, 53.33% and 75% respectively. In the post treatment cases, primary group of nodes was involved in 5 patients and secondary group in 4 patients. Among the patients with secondary nodes involvement, inguinal nodes were involved in 2 patients, paraaortic nodes in one patient and common iliac nodes in 2 patients. In our study, altogether 22 patients showed lesion on MRI. All cases showing diffusion restriction on MRI were diagnosed as recurrent lesions. (50) So, the number of patients showing lesions on T2 W, DWI, and contrast studies are 24,22 and 18 respectively. 4 patients showed T2 hyperintensity and diffusion restriction in cervix. However, on contrast study, there was poor enhancement of the tumour in these cases. Three patients showed T2 shine through effect on post radiation therapy MRI. They were imaged after 1 week, 3 months and oneyear of radiotherapy but no diffusion restriction was noted. Another patient who came for routine follow up and had no clinical features of recurrence showed mild enhancement of cervix on contrast. However, no lesion was detected on T2 W or diffusion weighted images. In one case, imaging was done 2 months after radiotherapy to assess the residual tumour which was clinically suspected. MRI of the patient showed no obvious lesion in T2 W images whereas diffusion restriction was noted with early arterial phase enhancement in dynamic contrast studies. Thus, a diagnosis of residual tumour was made for the patient. A combination of T2 W imaging and DWI is able to diagnose all the 22 cases and also excludes the 2 false positive cases in T2 W imaging. A combination of T2 W imaging and contrast study failed to diagnose 4 lesions showing diffusion restriction.

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Figure 1:Distribution Of Cases

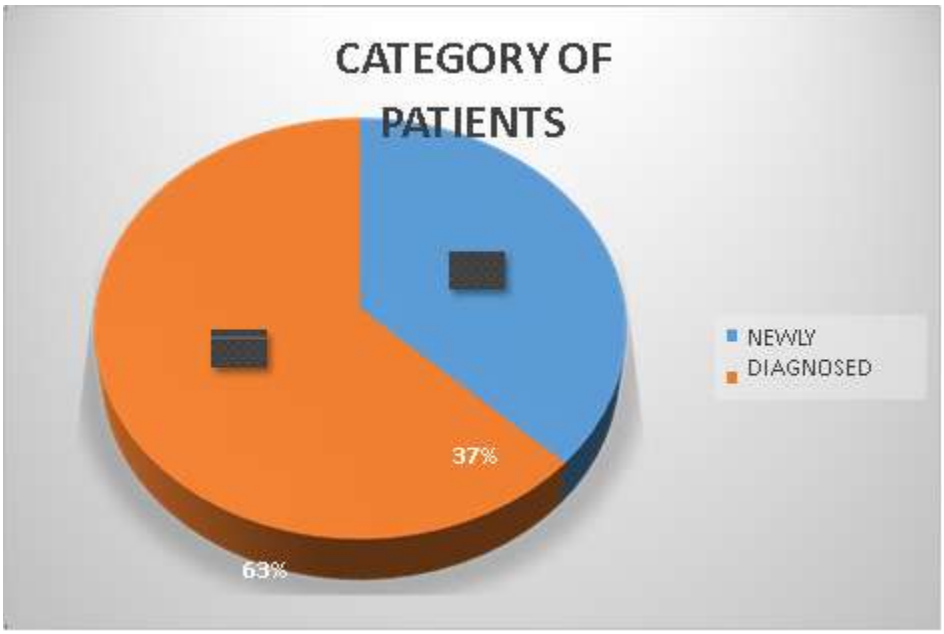

Figure 2: Common Presenting Symptoms

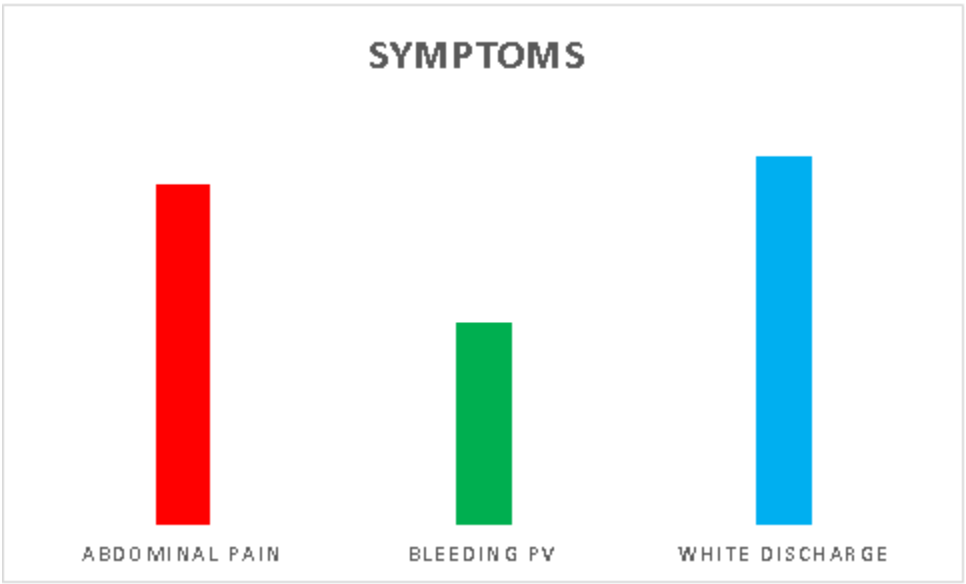

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Figure 3: Interval Between Rt And Imaging

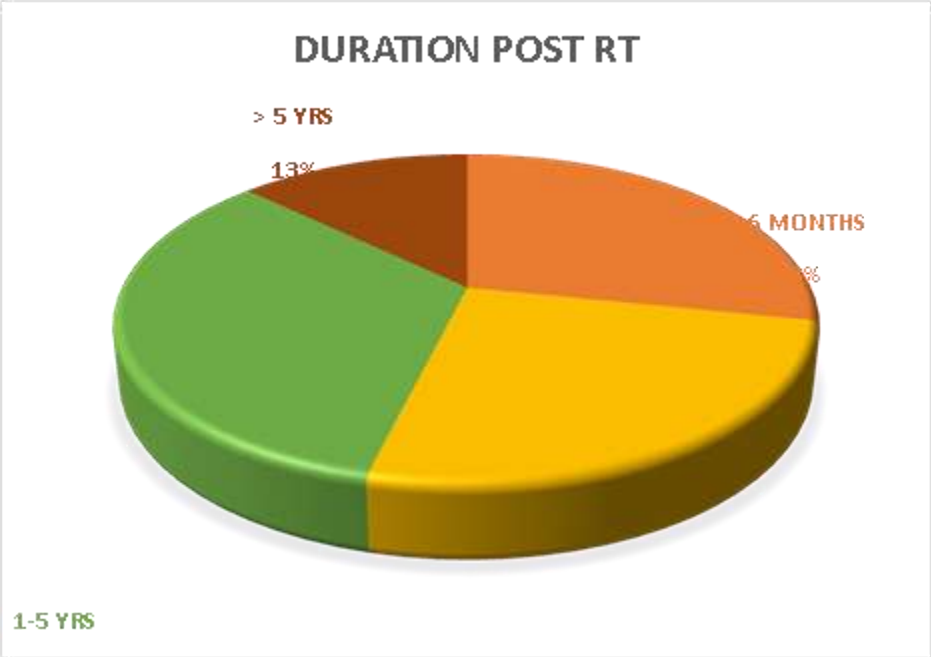

Figure 4:Hydroureteronephrosis

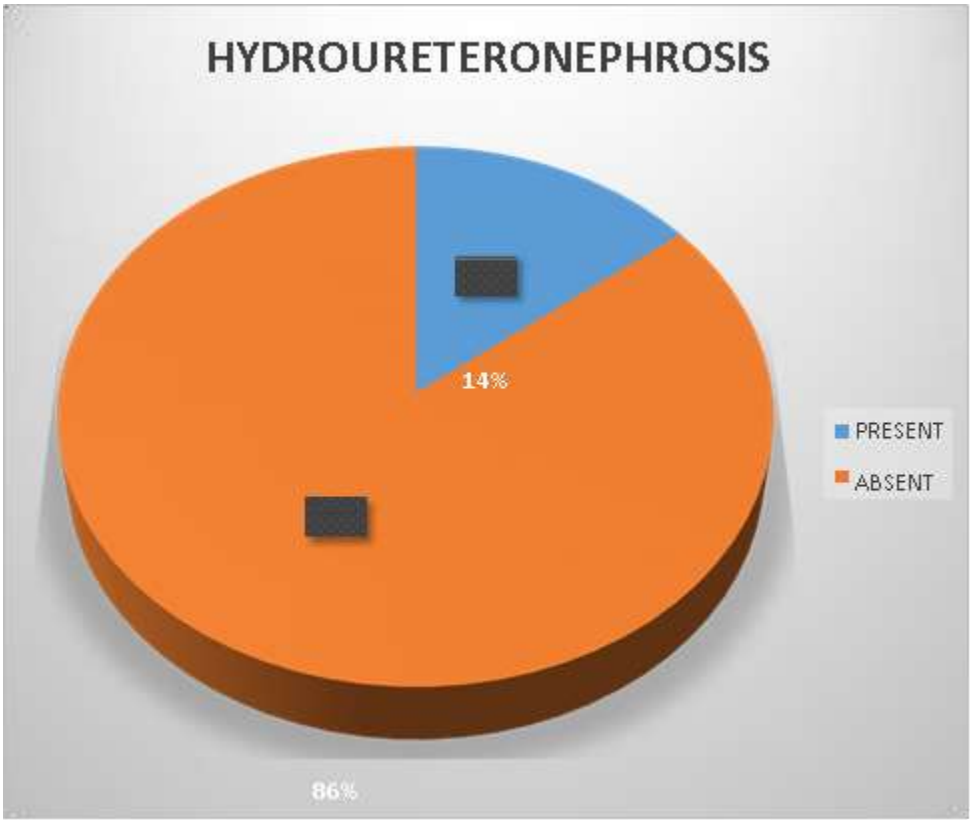

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Figure :5 : Correlation Between Hydrometra And Presence Of Mass

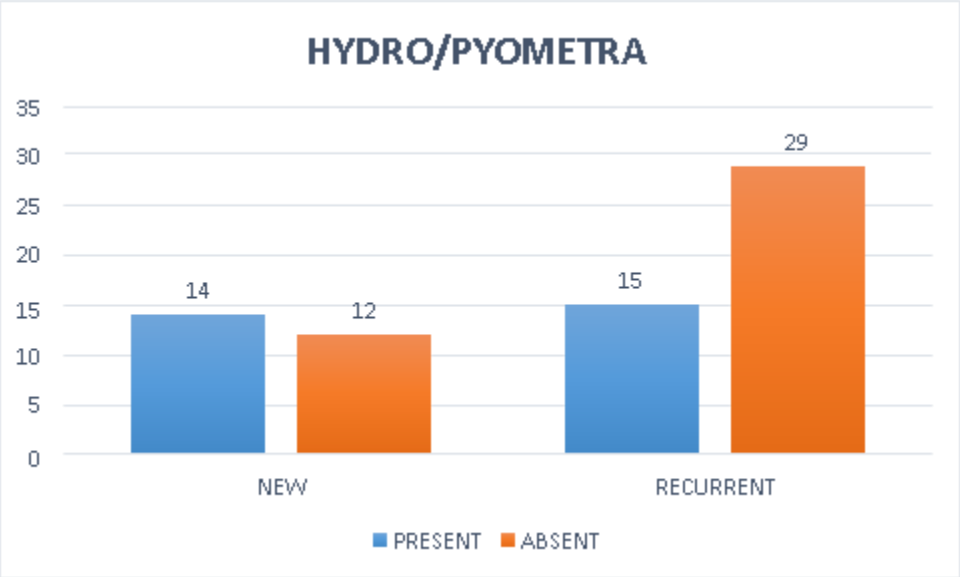

Figure 6: Correlation Between Clinically Suspected Mass And Positive Mri Findings

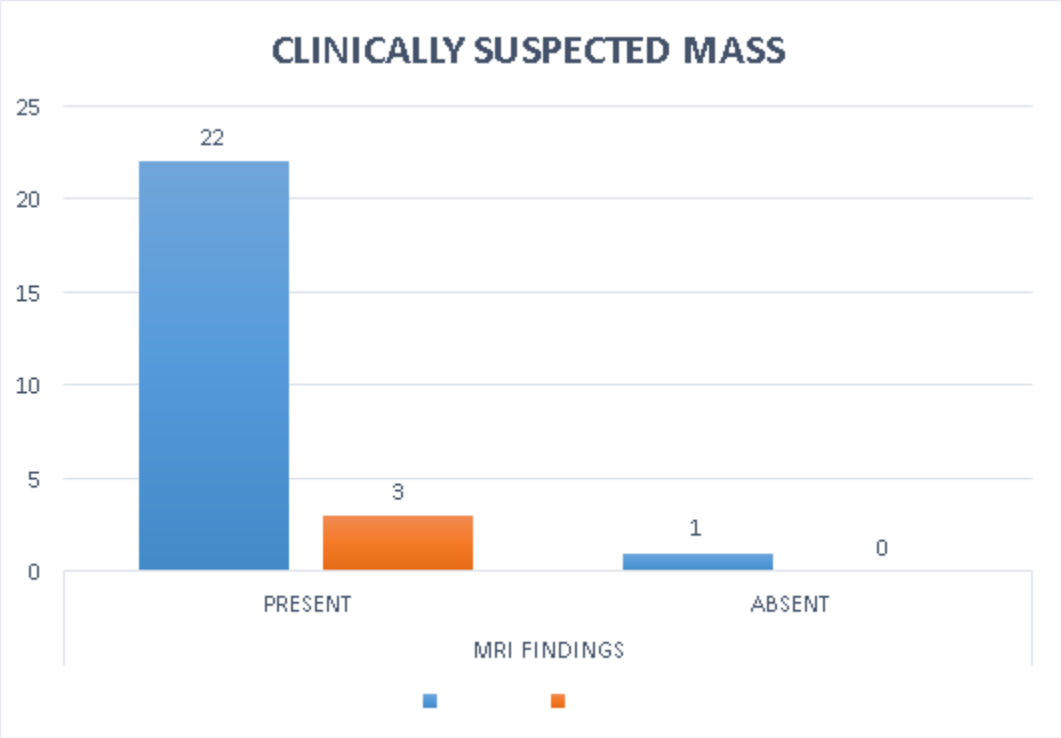

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Figure :7 Clinical Vs Mri Staging

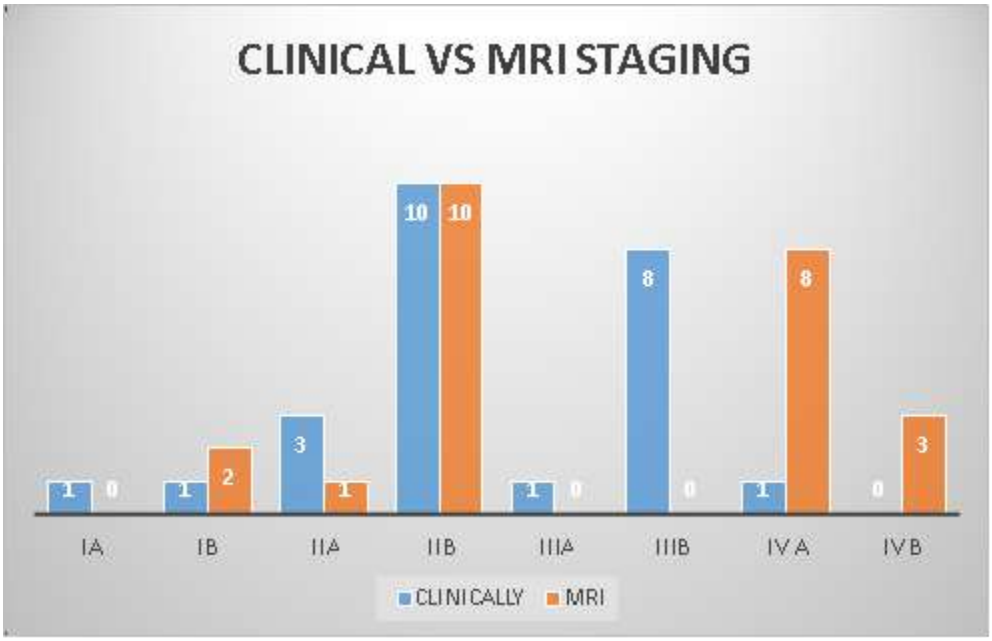

Figure :8 Positive Mri Findings In Different Sequences

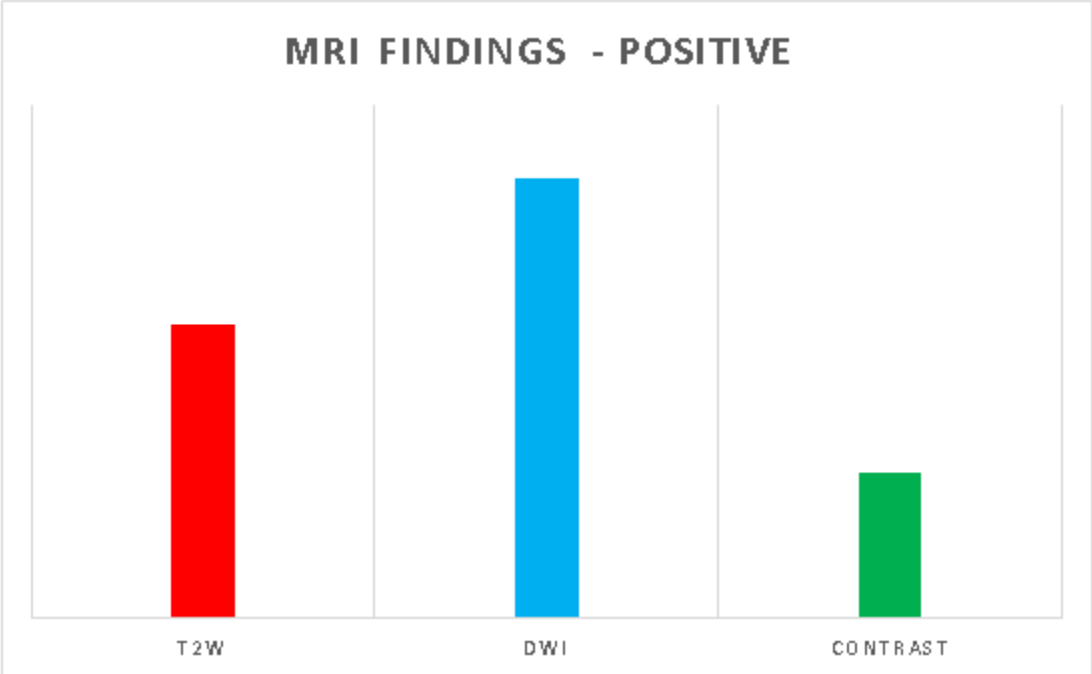

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FIGURE : 9STAGING CORRELATION WITH MRI

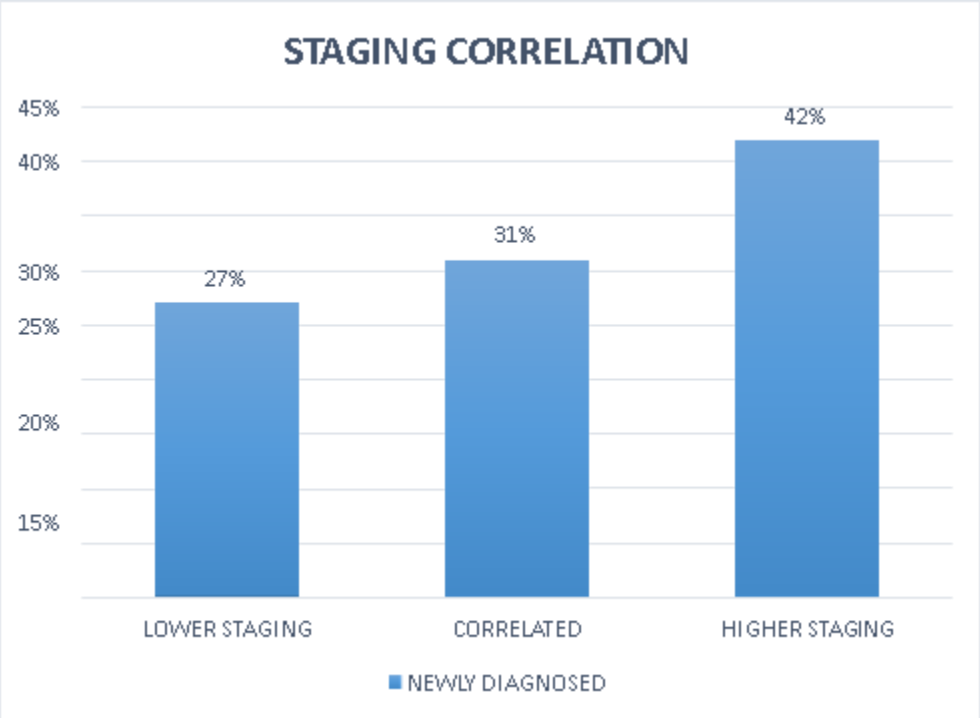

FIGURE 10:MRI FINDINGS VS CLINICAL MASS

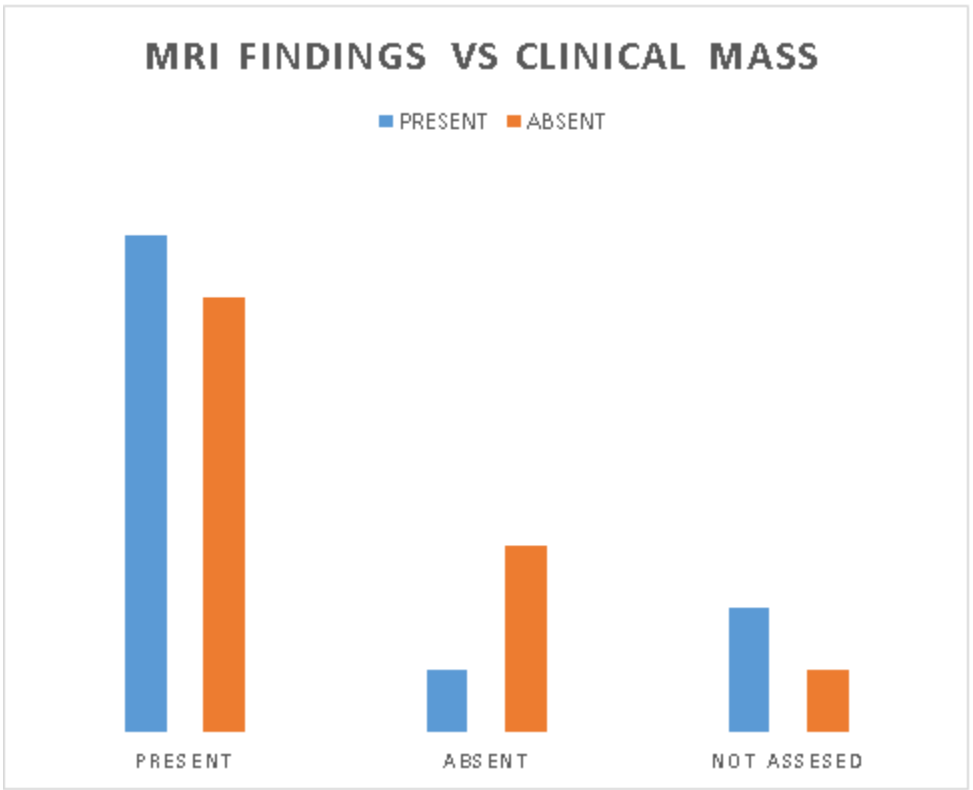

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Figure 11: Correlation Of Uterine Body Involvement With Mri Staging

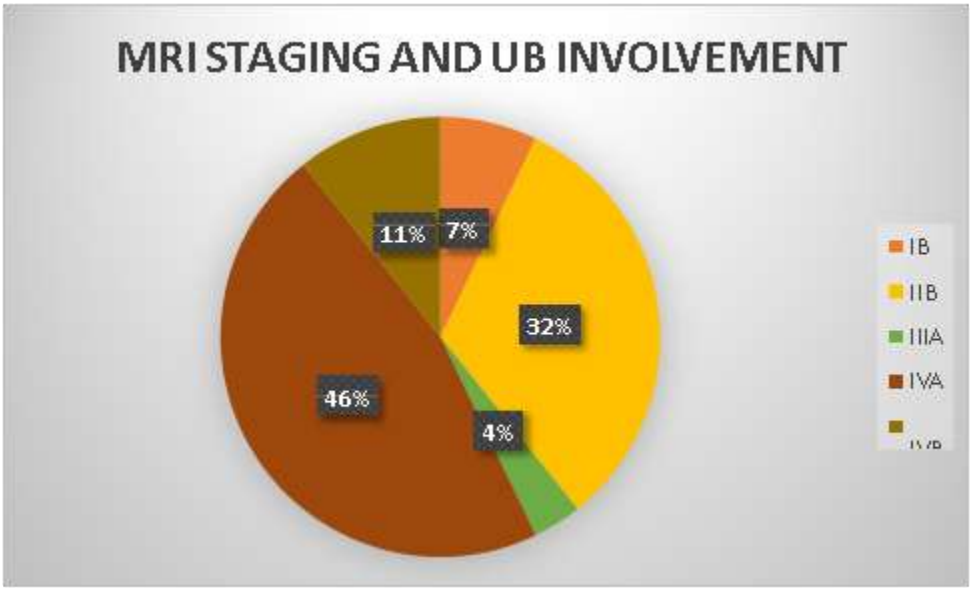

Table 12: Correlation Between Uterine Body Involvement And Lymph Nodes

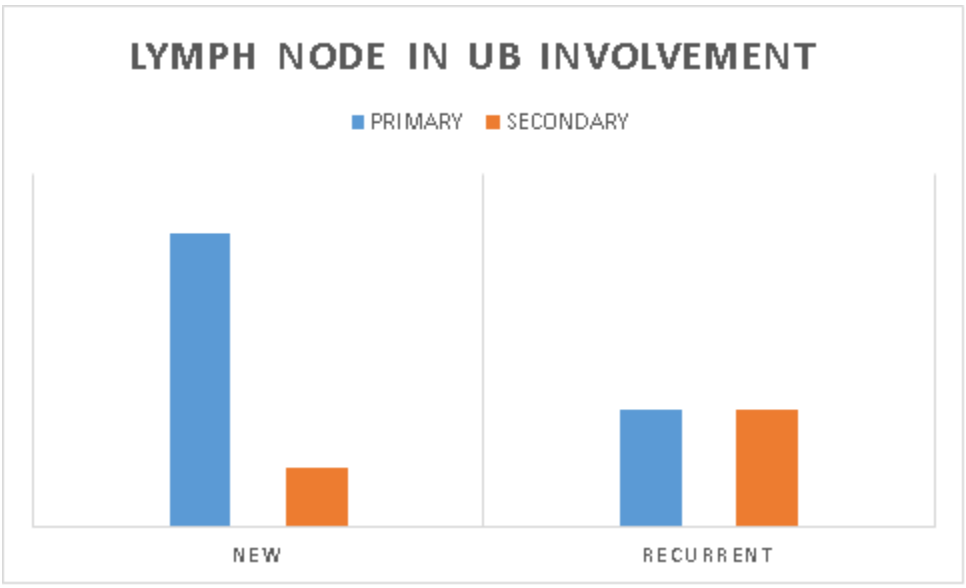

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Figure 13: Correlation Between Mean Size Of Tumour And Staging

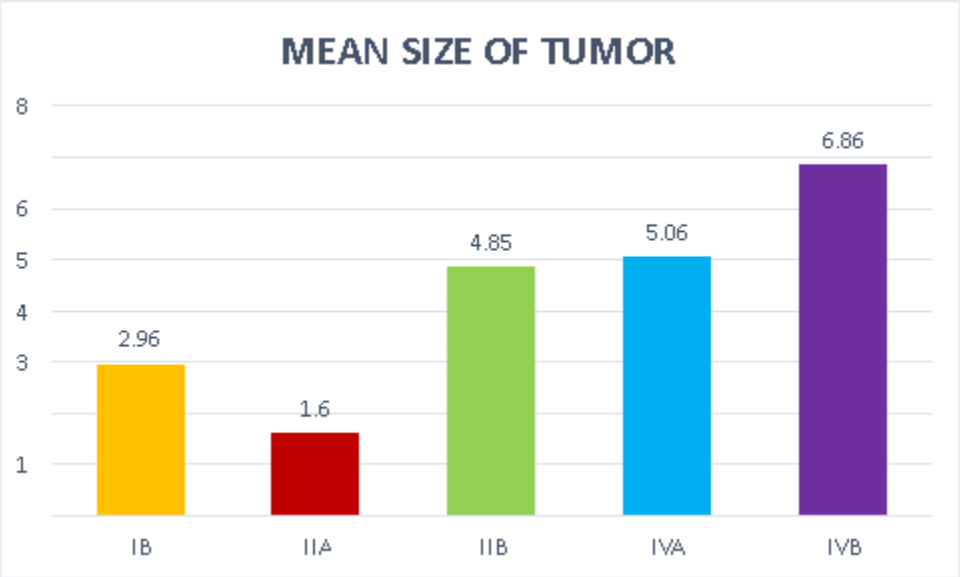

Figure 14: Post Radiation Complications

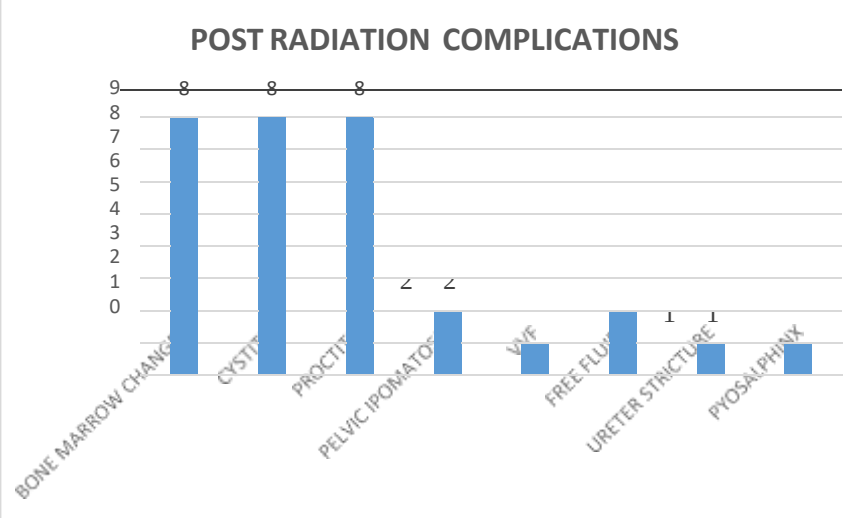

TABLE 1: OVERALL EFFICIENCY OF MRI SEQUENCES

FINDINGS PRESENT	NEW(N=26)	RECURRENT(N=44)
T2W	25	25
DWI	25	22
CONTRAST	23	18

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T2W+DWI	24	21
T2W+CONTRAST	23	17

TABLE 2: CORRELATION BETWEEN CLINICAL AND MRI STAGING IN NEW CASES

NEWLY DIAGNOSED	**MRI STAGING**		
CLINICAL STAGING	**LOWER STAGING**	**CORRELATED**	**HIGHER STAGING**
1A	1	0	1
1B	0	0	1
IIA	1	0	2
IIB	2	7	1
III	3	0	6
IV	0	1	0
TOTAL	**7**	**8**	**11**

Discussion

Two categories of patients are considered for study- 26 newly diagnosed patients (37% of study population) and 44 treated cases (63% of study population)The most common presenting symptom is white discharge according to our study (seen in 57% of the study population) followed by lower abdominal pain (seen in 53% of patients).[9] Among the new cases diagnosed, majority of them belonged to age more than 60. But, among the recurrent cases, the common age group is 41- 50 years. These patients must have been diagnosed with disease at an early age. Thus, it is seen that when the life expectancy is more, the possibility of recurrence of tumor is also more.[10]The most common histopathological type was squamous cell carcinoma in both newly diagnosed and recurrent cases.In our study, majority of the patients belonged to post menopausal age group. Thus, the disease is more prevalent among post menopausal women.[11]According to our study, the average time of disease free survival after therapy was about 2.5 years.In our study, totally there are 26 biopsy proven new cases. Clinically mass was identified in 23 cases and was not diagnosed for 3 cases.However, MRI showed the presence of mass in 25 cases. It was also noted that accurate staging was lacking in cases who underwent hysterectomy for early stage disease and for benign reasons.[12] These patients would be benefitted with MRI. The accuracy, sensitivity, positive and negative predictive values of MRI in newly diagnosed cases are 88.19%, 88%, 92.59% and 95.65% respectively.MRI without

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contrast is reliable in assessing the parametrium and pelvic side wall invasion. T2 W images give good information. MRI scores better in delineating the invasion of adjacent organs. In our study, significantly, 8 cases which were diagnosed as stage IIIB clinically were found to be stage IV A with MRI. Two cases of clinically staged IIA were actually found to have bladder invasion on MRI and hence staged as IV A. MRI evaluation prevented unnecessary surgical intervention in these patients. [13]Invasion of bladder and rectum can be ruled out with sufficient confidence with MRI. For all the newly diagnosed cases staged with FIGO system using clinical examination and MRI, correlation was the best for stage II B disease and higher staging was given with MRI to clinical stage III disease. MRI staging correlated with clinical staging in 31% of new cases and there was up staging with MRI for 42% of cases and down staging for 27% of cases.[14] This was due to the reason that all the stage III disease patients diagnosed clinically had minimal bladder wall/ rectal wall invasion which was missed and the cases were misclassified. So MRI is advocated in all advanced cases for proper staging and prognostication.From our study, it is evident that there is no definite role for contrast study in all the cases which are newly evaluated. There is no added advantage of contrast over plain study. DWI- MRI was able to diagnose 96% of cases and T2 W and contrast images detected 92% cases.[15] Among the 26 newly diagnosed cases (biopsy proven), T2 W, DWI and contrast enhanced imaging showed lesions in 24, 25 and 23 cases respectively. A combination of T2 W and DWI detects lesion in 24 cases. A combination of T2 W and contrast imaging diagnosed 23 cases and missed 2 cases. This finding is also in concordance with the study by Lucas et al., who reported a higher accuracy for the combination of T2 WI and DWI in the diagnosis of the lesion.[16] In our study, primary group of lymph nodes (parametrial, obturator,external and internal iliac nodes) was involved in 6 patients (23%) among the newly diagnosed. Secondary group of lymph nodes was involved in 3 patients. (11.5%). From our study involving post treatment cases, it is clearly evident that there is no added value of routine contrast imaging for all post radiotherapy cases. It has an added value in case of discrepancies between findings inT2 W imaging and DWI where it serves as a problem solving tool. In our study, altogether 22 patients showed lesion on MRI. The number of patients showing lesions on T2 W, DWI, and contrast studies are 24, 22 and 18 respectively.[17] The accuracy, sensitivity, specificity, positive and negative predictive values of MRI in recurrent cases are 57.89%, 88.89%, 30%, 53.33% and 75% respectively.In the post treatment cases, primary group of nodes was involved in 5 patients and secondary group in 4 patients.The most important prognostic indicators are size of the tumor, uterine body involvement by the tumor and nodal metastasis.[18]More number of cases with stage IV disease are found to have uterine body involvement in our study. Thus, uterine body involvement could be directly correlated with advanced stage of the disease. In our study, the uterine body involvement could be positively correlated with lymph nodal metastasis with a significant “p value” of 0.025. Thus, among the 28 cases with uterine body involvement, 7 patients showed primary lymph node metastasis and 3 patients showed secondary lymph nodal metastasis[19].Mean size of the tumor is another important prognostic factor as this could be correlated with the stage of the disease and nodal involvement. The mean size of the tumor correlates well with tumor staging in stages greater than IIA. It is also noted that there is nodal involvement if the mean size of the tumor crosses 5.67 cm.[20]In one third of post treatment patients, the hydrometra is due to cervical stenosis, a complication of radiation therapy.From our study, it is evident that post radiation complications are more common to develop after 2-3 years of radiotherapy which also corresponds with the average time of recurrence. Since most of the patients are referred during this time to look for recurrence of tumor, more complications are also diagnosed during this time. The most common post radiotherapy changes are fatty replacement of bone marrow followed by cystitis and proctitis.[21,22]

Conculsion :The most important prognostic indicator was the uterine body involvement in patients with carcinoma cervix. Uterine body involvement could be directly correlated with advanced stage of the disease and it is also associated with nodal metastases. Among the post treatment cases, hydrometra was more commonly associated with cervical mass. Only a few showed cervical stenosis. Nodal involvement is

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another important prognostic factor. Both in new and post treatment cases, primary group of nodes was more commonly involved than secondary group. Mean size of the tumor was another important prognostic factor as this could be correlated with the stage of the disease and nodal involvement. The mean size of the tumor correlated well with tumor staging in stages greater than IIA. It was noted that there was nodal involvement if the mean size of the tumor crossed 5.67 cm and it was not seen in cases where the mean size of the tumor was 4.57 cm or lesser.From our study, it was evident that post radiation complications were more common to develop after 2-3 years of radiotherapy which also corresponded with the average time of recurrence. The most common post radiotherapy changes were fatty replacement of bone marrow followed by cystitis and proctitis.

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