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Treatment Outcomes of Cobalt-60 Source Based High-Dose-Rate Intra-Cavitary Brachytherapy for Cervical Cancer

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Abstract: ***Background and Objectives: Best survival rate in carcinoma cervix is achieved when EBRT and brachytherapy are used. HDR has largely replaced LDR which was standard system of ICBT. With introduction of after-loading technology, HDR delivery became safe and more precise than LDR brachytherapy. Recently, miniaturized size of Co ^{60} sources has been made available with identical geometric and dosimetric properties as those of Ir ^{192}. So, Cobalt-60 is a more economical and logistic option for low resource settings like ours. This study aimed to evaluate treatment outcomes carcinoma cervix patients following HDR ICBT with Co-60 source in terms of Acute & late gastrointestinal & genitourinary toxicity, and Local disease control. Methods: Prospective observational study conducted on carcinoma cervix patients who received upfront EBRT with concurrent chemotherapy followed by HDR ICBT using Co-60 source. Acute and late gastro-intestinal and urogenital toxicities were evaluated using RTOG criteria. Treatment response was assessed using RECIST 1.1 criteria. Results: Majority of the patients (75%) had large tumors. 7.7% of patients had ≥grade 2 upper gastrointestinal toxicities. 25% developed higher grades of acute lower gastrointestinal toxicity. 5.8% developed ≥2grade of acute genitourinary toxicity. 1 patient developed intestinal obstruction. 93.3% developed only lower grades of late genitourinary toxicity. Complete response was observed in 84.5% of the patients, Partial response in 11%. Conclusion: HDR brachytherapy with newly installed cobalt source yielded acceptable toxicity rates and reassuring response rates. It can be considered as a reliable and cost-effective alternative to existing iridium-192 source.***

Keywords: Brachytherapy, cobalt 60, cervix, radiotherapy

1. Introduction

Cervical cancer is the **most common gynaecologic cancer worldwide and the 4th most common malignancy** in women after breast, colorectal, and lung cancers (1). It is the second most common malignancy among females in India(2). Every year over 500000 cases are diagnosed & 250000 die of the disease globally (3). 85% of cervical cancer incidences occur in underdeveloped nations, where it is the most common cancer-related death in women(4). The most significant contributing factor to the emergence of cervical cancer is persistent human papillomavirus (HPV) infection(5,6). A history of smoking, parity, oral contraceptive use, early age of coitus, multiple sexual partners, history of STDs, specific autoimmune illnesses, and chronic immunosuppression are other epidemiologic risk factors linked to cervical cancer (7, 8).

The best survival rate is achieved when EBRT and brachytherapy are used for the treatment of cervical cancer, one of the cancers that can be efficiently cured by radiation(9). According to ICRU Report 38, there are three different types of brachytherapy: LDR, MDR, and HDR, each with advantages and disadvantages(10). The three types of brachytherapy are: low-dose rate (LDR), which has a dosage rate between 0.4 and 2 Gy/h, medium-dose rate (MDR), which has a dose rate between 2 Gy/h and 12 Gy/h, and high-dose rate (HDR), which has a dose rate greater than 12 Gy/h (10).

External beam radiation covers the primary cervical tumour; treats any adjacent parametrial or uterosacral, uterine, or vaginal extension; and, addresses microscopic disease present in pelvic lymph nodes. In order to maximise tumour control when treating invasive uterine cervix cancer, it's crucial to administer sufficient doses of radiation to both the primary tumour and the pelvic lymph nodes. The initiation of external beam radiation typically precedes brachytherapy. Many institutions prefer to wait until the end of EBRT before beginning brachytherapy, especially for patients with large

tumours, as the brachytherapy dose to the normal tissues may be better optimised after maximal tumour shrinkage (3).

According to National Comprehensive Cancer Network Guidelines (2010), the primary treatment for locally advanced cervical cancer is definitive radiotherapy with concurrent cisplatin-based chemotherapy(11). Cisplatin-based chemotherapy delivered concurrently with external beam radiation reduces local recurrence and improves overall survival (12–18).

The total treatment duration of EBRT and brachytherapy should be limited to less than 8 weeks, as prolonged treatment duration leads to a decrease in local control and survival of approximately 1% per day(19–22).

ICRT is a form of conformal dose escalation with a higher therapeutic ratio and can deliver a high radiation dose to the microscopic or macroscopic residual tumour after EBRT while sparing the adjacent normal organs such as bladder and rectum; thereby reducing the risk of residual cancer and pelvic relapse (23–27). Therefore, in patients with locally advanced disease (stages IB_2 to IIIB) brachytherapy is a standard part of treatment after external beam radiation (28).

In carcinoma cervix, the response to radiotherapy is dose dependent i.e., as the dose increases the probability of tumour control also increases but this comes at an expense of higher late toxicities to the normal surrounding structures. This concept applies to both overall dose for LDR and dose per fraction for HDR(27).

High dose rate (HDR), and low dose rate (LDR) BCT are relatively equivalent based on the results from various retrospective and prospective studies(27,29–36).

Acute toxicity are acute reactions following treatment and are rapid in onset and typically reversible. These occur from day 1 of commencement of therapy to day 90 according to Radiation Therapy Oncology Group (RTOG) definition.

Late toxicity reactions are those observed after 90 days of commencement of therapy.

LDR which was traditionally the standard system of intracavitary irradiation has now been largely replaced by HDR in most of the centres. With the introduction of after-loading technology, HDR delivery became safe and more precise than possible with LDR brachytherapy. The main concern with HDR therapy is the potential late toxicity because of large dose per fraction(27,37–39).

The disadvantages of LDR and MDR brachytherapy are prolonged treatment time that may lead to displacement of the applicator and increased risk of thromboembolism; and unnecessary radiation exposure to the radiotherapy personnel. HDR brachytherapy on the other hand is an outpatient treatment with better patient compliance due to lesser treatment time and avoidance of hospitalisation, prolonged immobilisation, discomfort due to vaginal packing and urinary catheterisation and thereby much advantageous than both LDR and MDR techniques(23,40–42). From the radiation oncologist's point of view, In terms of maintaining crucial spatial linkages between the treatment applicator and the dose-limiting normal surrounding structures during brief treatment times, higher patient turnover, and cost effectiveness, HDR brachytherapy is very favourable. (42). In developing countries like ours, HDR brachytherapy is a boon for government hospitals catering to large patient populations within stipulated time. The shorter treatment time in HDR technique does not allow for sub-lethal damage repair during irradiation but if interval of more than 24 hours is maintained then the normal tissues can undergo full repair(27,43). With HDR treatment, the tumor shrinks between insertions, allowing reoxygenation of areas of chronic hypoxia. The oxygen enhancement ratio is lower for LDR than for HDR(27,44). HDR brachytherapy has been utilised successfully for the past 40 years, and majority of the centres showed similar local control, survival, and morbidity to those of LDR (37).

Over a dozen radioactive nuclides have a history of use as sealed sources in brachytherapy. HDR brachytherapy requires an intense source but with a size that can pass through the needles placed in a tumor.

Traditionally HDR afterloaders have been based on Iridium ^{192} or Cobalt ^{60} (23). Ir ^{192} radionuclide source has been widely used for HDR because of the ease to manufacture it in smaller size for intracavitary applications owing to its high specific activity. Co-60 based HDR was though available but unpopular because of its larger size sources(24). Recently, miniaturized size of Co ^{60} sources has been made available with identical geometric and dosimetric properties as those of Ir ^{192}.

The potential advantage of using Co ^{60} is its longer half-life of 5.3 years compared with 74 days of Ir ^{192}, thus, extending the time between source changes from 3-4 months to approximately 5 years(28). It will take 15-20 Iridium Sources (which will cost around 4.5 lacs per source leading to 90 lacs for 20 sources) for the period in which One Cobalt source is replaced (having cost of 45 lacs). Therefore, there will be a saving of 40-45 lacs. This represents a more economical and logistic option for low resource settings like ours. On the other hand, the higher energy of Co ^{60} requires considerably more shielding and raises the concerns for possible increase in toxicity.

Comparative studies have shown similarity of physical dose distributions in carcinoma cervix for Cobalt-60 and Iridium-192(45,46). However, the biological dose distributions, as opposed to the physical dose distributions, are more closely related to the clinical results, such as localised tumour control or nearby normal tissue harm. The relative biological effectiveness (RBE) and healing of sublethal damages during irradiation, which depend on the source energy spectrum and dose rate, respectively, have an impact on the biological dose, which in turn has an impact on the physical dose(46,47). Due to imprecise assumptions like the fact that all high-energy photons are classified as low linear energy transfer (LET) radiations

with RBE = 1, the HDR dose fractions are delivered more quickly relative to damage repair half time so that intrafraction repair can be neglected, the biological differences between these two sources were thought to be largely insignificant despite the fact that both the energy spectrum and dose rate are different (46).

During radiotherapy treatment for cervical cancer, up to 84% of patients exhibit some form of acute radiation toxicity(48–51). The most common manifestations are gastrointestinal, genitourinary toxicity and hematological. These unfavourable radiotherapy side effects vary in strength and severity depending on the radiation dose, fractionation schedule, radiation technology used, and length of treatment(50,51). The patient's unique traits, the disease stage, genetics, comorbidities, and other therapy modalities used are known to interact and function as determinants(51–55). The emergence of serious acute radiation toxicities is one of the most important causes of the development of chronic toxicity, which frequently necessitates extensive intervention and the rising costs of long-term treatment. There is therefore plenty of motivation to concentrate on the accurate and prompt identification of patients who are more likely to have acute radiation induced toxicities and their ongoing surveillance.

Treatment results of HDR brachytherapy for carcinoma cervix using Ir ^{192} radionuclide source is widely discussed in the literature but reports on studies with Co ^{60} are scanty and are mostly retrospective reviews.

We conducted this study on the newly installed brachytherapy unit in our institution to assess the treatment outcomes of HDR intracavitary brachytherapy with Cobalt-60 as radioactive source in cervical cancer patients.

This study aimed to evaluate the treatment outcome in patients of carcinoma cervix following HDR intra-cavitary brachytherapy with Co-60 radionuclide source in terms of:-
1) Acute & late gastrointestinal & genitourinary toxicity, and
2) Local disease control

2. Review of Literature

Frank C.S. Wong, Stewart Y, et al. (2003) (56) concluded that treatment results and complication rates of HDR remote after-loading brachytherapy using either Co ^{60} or Ir ^{192} sources for cervical cancer were comparable with those of the LDR series.

Atara I. Ntekim et al. (2014) (57) did a prospective study on 70 patients to evaluate the acute and late gastrointestinal and genitourinary toxicity associated with cobalt-60 source in the brachytherapy of cervical cancer using CTCAE criteria. The dose was 19.5Gy in 3 weekly fractions. Twice weekly treatment was allowed if inter fractional separation was atleast 72 hours. They concluded that the acute and late complications with Cobalt-60 HDR brachytherapy were similar to those reported for Iridium-192 and that Cobalt-60 HDR brachytherapy is tolerable, effective and economical for low resource settings.

Jain Abhay Kumar et al (2017) (58), did a prospective study on 65 patients to evaluate acute gastrointestinal and genitourinary toxicities using CTCAE criteria associated with cobalt-60 source in HDR-ICRT of carcinoma cervix patients and its comparison with iridium based source. EBRT 45-50 Gy/25# @ 1.8 or 2 Gy per fraction was delivered 5 days a week using telecobalt machine. 3 sessions of ICRT with dose of 7 Gy per fraction were delivered 72 hours apart. In their study, they concluded that the acute gastrointestinal and genitourinary toxicities of high dose-rate intracavitary brachytherapy using Co-60 radionuclide source is low and comparable with Iridium-192. Additionally, Cobalt-60 has economic advantage over Ir-192. Thus, it is more suitable for low economic resource settings.

Two Japanese studies compared Cobalt-60 HDR to Cesium-137 LDR brachytherapy, both given with external beam radiation found no differences in cause-specific survival (CSS), but late complications were higher with HDR in the study by Teshima et al (31,33,59).

A trial from India by Patel et al (1994) (29) used similar techniques as the abovementioned studies and found similar local control (LC) and survival for LDR and HDR, but reduced grade 1-2 rectal complications with HDR.

Afshin Raksha, Amir Shahram Yousefi Kashi, et al. (2015) (23) did a cross sectional analytic study to report outcome of 154 patients with carcinoma cervix who were treated with EBRT and HDR-BCT with cobalt-60 remote after-loading system. They showed that Co-60 as HDR source was successful after EBRT with acceptable rectal and bladder complications.

Thanatip Tantivatana, Kanisa Rongsriyam et al (2018)(24) did a retrospective cohort study of patients with cervical cancer and treated with brachytherapy using Ir-192 and cobalt-60. They concluded that cervical cancer patients who were treated with HDR Co-60 brachytherapy were comparable in survival and toxicity outcomes of those with HDR Ir-192 brachytherapy. Co-60 source has many economic advantages over Ir-192 and is suitable for low resource radiotherapy setting.

Viswanathan et al. (2012) (60) in a survey of the gynecologic cancer intergroup concluded that, with the use of HDR-BCT, there is significant variation among different centres with respect to the total tumour dose, dose per fraction and the proportion of tumour dose delivered with external beam radiotherapy (EBRT), versus that delivered by BCT.

Alexander J. Lin et al (2018)(59) concluded that there was no difference in local control with either LDR or HDR brachytherapy. The late complication rate was reduced with HDR and 3D-planned brachytherapy compared to LDR and 2D-planned brachytherapy.

Shirley Chibonda et al (2021) (61) did a retrospective analysis of data from records of patients with histologically confirmed cervical cancer treated with HDR-BT in Zimbabwe. They concluded that brachytherapy using high dose rate cobalt 60

sources in addition to external beam radiotherapy provided safe, well tolerated treatment with low numbers of grade 3 adverse effects.

Petra Selke (1993) (42) conducted a prospective study on treatment results with HDR-BCT using cobalt source in cervical cancer patients to evaluate the long term treatment results in terms of local disease control, survival and complications. They concluded that combined RT and HDRB is an effective, safe and practical treatment with a high degree of acceptability to patients and clinicians alike and 2 to 3 HDRB insertions, each delivering 800 to 1000 cGy to 100% of the prescribed Point A dose was associated with good local control and survival and an acceptable incidence of late toxicity.

Lorvidhaya et al (2000) (62) in their retrospective analysis of 2063 patients with histologically proven carcinoma of cervix treated by EBRT and HDR ICBT to evaluate disease free survival rates and late radiation induced toxicities. They concluded that HDR brachytherapy produced pelvic control and survival rates comparable to other LDR series.

Mohsin Khan et al (2022) (63), studied records of 472 patients with cervical carcinoma who were treated with curative intent concurrent chemoradiotherapy followed by HDR-ICBT using iridium-192 based source comparing two schedules of 6.6Gy per fraction for 4 doses or 8 Gy per fraction for 3 doses prescribed at point-A. They also reported late GI and GU toxicities suffered as the worst toxicity by the patients. They concluded that 8 Gy per fraction HDR brachytherapy dose in 3 applications is effective and safe for treatment of carcinoma cervix patients.

Montien Pesee et al (2010) (67), in their retrospective analysis on HDR-BT using cobalt-60 source in cervical cancer patients concluded that combined teletherapy along with high dose rate Cobalt -60 brachytherapy of 850 cGy/fraction, weekly to point A for 2 fractions resulted in overall 3.5% residual disease and a 96.5% complete response.

Om Prakash Gurjar et al (2016) (64), in his case series on dosimetric analysis of cobalt 60 source based HDR brachytherapy concluded that Co-60 HDR brachytherapy unit is a good choice especially for the centers with a small number of brachytherapy procedures as no frequent source replacement is required like in an Ir-192 HDR unit.

Upendra Nandwana et al (2015) (65)in their retrospective analysis found that dosimetry with Co-60 as a brachytherapy source was consistent with the ICRU 38 recommendations and concluded that Co-60 is a logical alternative to Ir-192 in low socio-economic settings when repeated changing of the source is not an option.

Stefan Strohmaier et al (2011) (66) compared the isotopes 60Co and 192Ir as radiation sources for high-dose-rate (HDR) afterloading brachytherapy in view of availability with identical geometrical dimensions and showed that no advantages or disadvantages exist for 60Co sources compared to 192Ir sources with regard to clinical aspects.

3. Materials and Methods

Study Design: It was a prospective observational study conducted on outdoor as well as indoor patients of carcinoma cervix, registered at our department during the period of December 2020 to November 2022.
Sample size was Thirty (30).

Patient selection

Inclusion Criteria
Histologically confirmed Squamous Cell Carcinoma of cervix**,** Newly diagnosed with no previous radiotherapy, chemotherapy or surgery for the same**,** Locally advanced, non-metastatic disease (FIGO Stage I_{B2} - III_B)**,** ≥ 18years of age**,** Normal baseline hematological, renal and hepatic profile, Karnofsky performance status of > 60.

Exclusion Criteria
Patients who refused to give consent or, withdrawal of consent at any stage of treatment, Histology other than Squamous Cell Carcinoma and its variants, Serious concomitant diseases, Prior or concurrent cancer in last 5 years, Pregnancy, HIV Seropositivity

Pre-treatment evaluation
History, physical and pelvic examinations, Routine blood counts, renal and hepatic profile, Chest X-ray, CT scan or MRI (contrast-enhanced) of abdomen and pelvis (as per indications), Cystoscopy and procto-sigmoidoscopy when clinically indicated

Consent
Procedure was explained to the patient in indigenous language and informed written consent was taken prior to enrolment in the study.

Ethical Clearance
Ethical clearance was obtained from the institutional ethical committee

Performance Status
Performance status was assessed using Karnofsky Performance Status (KPS) (ANNEXURE- 1).

Socio-Economic Status
Socio-economic status was assessed using Modified Kuppuswamy Scale in which both subclasses of middle and lower socio-economic status were merged into one class respectively. (ANNEXURE-2)

52 Patients who completed their EBRT with concurrent chemotherapy, 3 ICRT treatments and met the inclusion and exclusion criteria were assessed for patient, tumour and treatment characteristics, acute and late toxicities and response. 7 patients were lost to follow up after the brachytherapy

treatment and thus, late toxicities and response could not be assessed in them.

Staging
All patients were clinically staged according to International Federation of Gynaecology & Obstetrics (FIGO) staging system 2018 (ANNEXURE-3)

Treatment Protocol
All the patients received upfront external beam irradiation followed by HDR intra-cavitary brachytherapy using Cobalt 60 source

EBRT and Concurrent Chemotherapy
EBRT was delivered to the whole pelvis through standard anterior and posterior parallel opposed portals. Patients with antero-posterior separation greater than 18cm were treated by four field box technique with an anterior, posterior and two lateral fields. A total dose of 45-50 Gy was given at 1.8-2 Gy per fraction, 5 fractions per week using Cobalt-60 teletherapy unit 'THERATRON-780C'.

Borders in 2 Field Technique (FIG NO. 1)
Superior border- L4-L5
Inferior border- lower border of obturator foramen or 2cm below the vaginal extent of the disease
Lateral border- 1.5- 2 cm lateral to the widest true pelvic brim

Borders in four field technique
Superior, inferior and lateral borders- same as AP-PA field
Lateral field- anterior border was placed anterior to the symphysis pubis while the posterior border was placed along the sacrum.
Patients were treated to mid plane dose on AP/PA fields and at isocenter on four field box technique.

Concurrent chemotherapy
Concurrent chemotherapy consisting of injection cisplatin 35 mg/m^2 was delivered weekly. Prior to each chemotherapy cycle evaluation for the hematological, biochemical and renal function was done. Patients first received pre-medication (Injection Dexamethasone, Injection Ranitidine and Injection Ondansetron) followed by which intravenous infusion of Injection Cisplatin 35mg/m^2 was administered over 2 hours with adequate hydration. After the administration of chemotherapy, patients received EBRT fraction of that day.

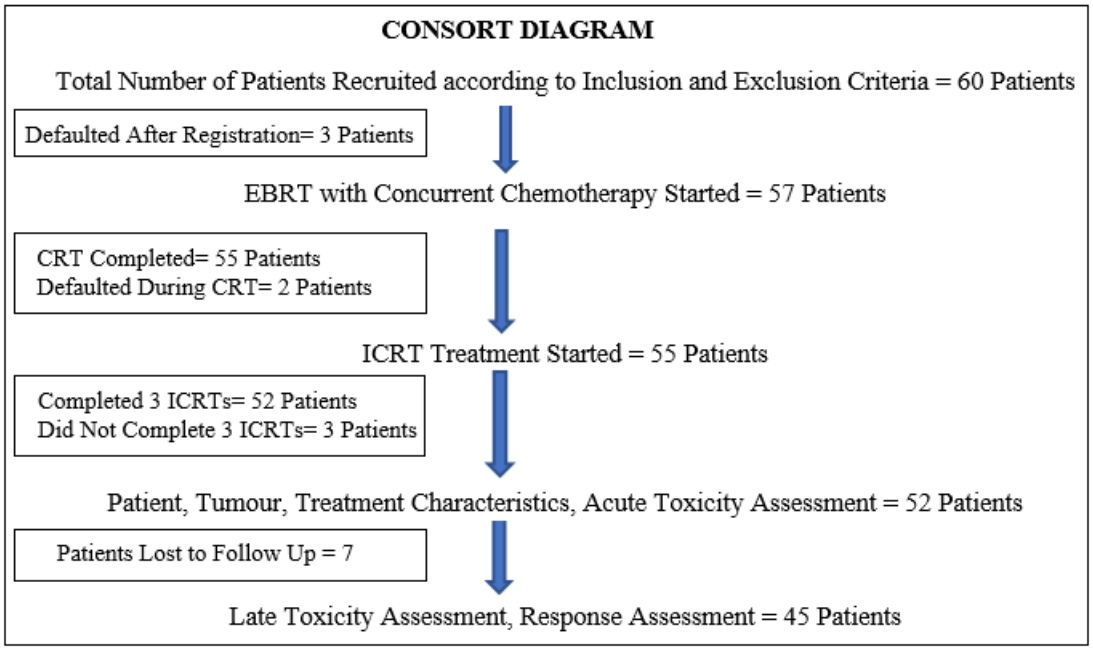
Intracavitary Brachytherapy (ICBT)
HDR ICBT was performed after the completion of EBRT after a gap of 1 week. A total of 3 treatments were planned for each patient at weekly interval. A Foley's catheter was inserted into the urinary bladder and the balloon inflated with 7 cc of diluted urograffin to identify the bladder neck region. Rectal marker was placed per rectally to localise the rectal point. The applicator system consisted of either Fletcher applicator with rigid tandem and paired ovoids (Fig No. 2) or ring applicator. The vagina was packed with gauze to further displace the bladder anteriorly and the rectum posteriorly to minimize the dose to these organs. AP and lateral orthogonal X-ray films were taken (Fig No. 4). The miniature Co-60 radioactive source available on remote after-loading equipment SAGINOVA by ECKERT & ZIEGLER BEBIG, Germany (Fig No. 3) dedicated to high dose rate (HDR) brachytherapy was used for intracavitary radiation. The dose per fraction was 8Gy to Point A. Dose prescription was to point "A". Multiple points consistent with ICRU 38 were located and used for treatment planning and dose optimization to point A, point B, bladder, rectum (Fig No.5)

Assessment

Acute and Late Toxicities
During the ICRT treatment course, patients were assessed weekly for normal tissue reactions and later as per the follow-up protocol. Acute and late gastro-intestinal and urogenital toxicities were clinically evaluated using the Radiation Therapy Oncology group (RTOG) toxicity criteria. (ANNEXURE-4). Worst toxicity developed by the patient during follow up was reported.

Response
Treatment response was assessed 6-8 weeks after completion of radiotherapy using RECIST 1.1 criteria (Annexure-5)

Statistical Analysis
Data was analysed using computer program Statistical Package for Social Sciences software (SPSS) version 25.0.



Follow Up

First follow up was done at the completion of radiotherapy as planned, then at 6 weeks followed by 2 monthly basis upto 6 months, then 3 monthly afterwards.

4. Results

Patient, Tumor and Treatment Characteristics

Median age of our study population was 55 years (35-71 years). 32.7% had co-morbidities like Hypertension, Diabetes Mellitus, and CAD etc. About four-fifth of the patients were post-menopausal. More than half of the patients belonged to low socio-economic strata. All of the patients had KPS either 80 or 90 (50% each). (TABLE I). About a third of the patients were in stage IIB and IIIB each. More than two-third patients had moderately differentiated squamous cell carcinoma. Majority of the patients (75%) had large tumors of >4cm (TABLE II). Maximum patients (69.2%) completed their treatment (EBRT + ICRT) in 56-63 days since there was a short time interval between EBRT and ICRT (<2 weeks), while for 30.8% of the patients, this interval was extended to 3-4 weeks, increasing the overall treatment time. About 65% patients received all 5 cycles of concurrent chemotherapy while 35% patients received <5 cycles due to tolerance issues (TABLE III).

Toxicity and Response Assessment (TABLE IV & V)

Acute Upper GI Toxicity: 92.3% patients developed only lower grades of acute upper gastrointestinal tract (grade 0, grade 1) who did not require any medications and were relieved on their own. Only 7.7% patients had ≥grade 2 toxicities who required intervention in the form of oral medications. Nausea was the most common acute upper gastrointestinal symptom observed by the patients followed by anorexia and pain abdomen. None of the patients developed grade 3 and 4 upper gastro-intestinal toxicities. Therefore, no surgical intervention was warranted for any patient. Grade 1 acute lower GI toxicity was observed in 25% patients, grade 2 in 23.1% patients and grade 3 in 1.9% patients

Acute Lower GI Toxicity: 75% of the patients developed only lower grades of acute lower gastro-intestinal toxicity and did not warrant any medication.

Only 25% of the patients developed higher grades of acute lower gastrointestinal toxicity requiring oral medications

Only 1 of them required parenteral fluid support for diarrhea induced dehydration with delay of 1 week in the brachytherapy treatment.

Rectal discomfort was the most common acute lower gastro-intestinal symptom observed by the patients followed by diarrhea and pain abdomen.

Acute GU Toxicity: Only 5.8% of the patients developed higher grades of acute genitourinary toxicity requiring local anesthetics.

Late GI Toxicity: Increased bowel frequency was the most common symptom observed by the patients followed by diarrhea and bleeding per rectum which were managed conservatively. 1 patient developed intestinal obstruction (grade 3 lower gastro-intestinal toxicity) after 12 months of treatment which was relieved by conservative management.

Late GU Toxicity: majority of the patients (93.3%) developed only lower grades of late genitourinary toxicity (grade ≤1) not requiring any medications.

Response Assessment (TABLE VI):

Complete response was observed in 84.5% of the patients, Partial response in 11%. Therefore, overall response rate observed was 95.5%. None of the patients had stable disease

status on evaluation. Progression of disease was observed in 2 patients (4.4%). 7 patients were lost to follow up and therefore were not available for response assessment.

5. Discussion

Cervical cancer remains a significant public health challenge in developing countries like India, where late presentation is common due to limited awareness, inadequate screening programs, and barriers to timely healthcare access. As a result, most patients are diagnosed at locally advanced stages, requiring combined modality treatment. The current standard of care for such cases includes external beam radiotherapy (EBRT) with concurrent cisplatin-based chemotherapy followed by high-dose-rate (HDR) intracavitary brachytherapy (ICBT).

While Iridium-192 (Ir-192) has traditionally been the most widely used source for HDR brachytherapy, Cobalt-60 (Co-60) offers distinct logistical advantages, especially in resource-constrained settings, owing to its longer half-life and reduced need for source replacement. However, clinical data on the efficacy and toxicity profile of Co-60-based HDR brachytherapy remain limited, with most existing studies being retrospective in nature. This study was conducted to evaluate the acute and late gastrointestinal (GI) and genitourinary (GU) toxicities, as well as treatment response, in patients treated with Co-60-based HDR ICBT at our institution.

Toxicity Profile

In the present study, the incidence of ≥Grade 2 acute toxicities was 7.7% for upper GI, 25% for lower GI, and 5.8% for GU toxicities. The majority of toxicities were low-grade and self-limiting, with only one patient requiring treatment delay due to Grade 3 diarrhea. Late toxicities were also minimal, with 9.9% of patients experiencing ≥Grade 2 late GI toxicity and 6.7% reporting ≥Grade 2 late GU toxicity.

Our toxicity findings are broadly comparable with prior studies. For instance, Ntekim et al. (57) reported Grade 2 or higher acute GI toxicity in approximately 20% of patients and only 3% experiencing Grade 3 diarrhea. Similarly, Jain et al. (58) reported ≥Grade 2 acute GI and GU toxicity rates of 11.9%, while Raksha et al. (23) observed Grade 3 GI and GU toxicity in 3.8% and 2.6% of cases, respectively. Our findings also align with Chibonda et al. (61), who reported low rates of ≥Grade 2 toxicity, and with Selke et al. (42), who reported late Grade 3–4 toxicity in 7.6% of patients, slightly higher than our observed rate.

Pesee et al.(67), in their retrospective analysis of Co-60-based HDR brachytherapy, reported Grade 1–2 proctitis in 37.6% and radiation cystitis in 2.8% of patients, with Grade 3 complications in under 1%. Mohsin Khan et al. (63) observed late ≥Grade 2 GI and GU toxicities in 9.4% and 4.2% of patients, respectively, which closely matches our outcomes. Similarly, Lorvidhaya et al.(62) reported Grade 3–4 bowel and bladder complications in 7.0% of patients, while Orton et al.'s meta-analysis(40) found a lower major complication rate with HDR (9.1%) than LDR (20.7%).

Grade 1/2 late rectal toxicities in our cohort are also consistent with those reported by Wang et al. (68) (39% for Grade 1/2) and Ogino et al. (69) (37.3% for Grade 1/2), although our incidence of Grade 3/4 toxicity was significantly lower, highlighting the favorable safety profile of Co-60 HDR in our setting.

Treatment Response

The overall treatment response was encouraging, with a complete response (CR) rate of 84.4% and an overall response rate (CR + partial response) of 95.5%. These results are comparable with several published series. Pesee et al. (67) reported a CR rate of 96.5% using Co-60, while Thanatip Tantivana et al. (24) found CR rates of 98.9% and 99% for Ir-192 and Co-60, respectively. Chibonda et al. (61) documented a 75% complete response rate at 6 weeks post-treatment, and Patel et al. (29) reported disease control in 70% and 67.3% of patients in the LDR and HDR arms, respectively.

Our response rates, although slightly lower than some Co-60 studies, remain within the acceptable range and exceed those reported in studies using Cesium-137. Variability in patient population, tumor burden, treatment duration, and follow-up period may explain the marginal differences in response rates.

Comparative Assessment

Taken together, our findings support the growing body of evidence that Co-60 is a clinically effective alternative to Ir-192 for HDR brachytherapy in cervical cancer. The toxicity and response outcomes observed in our study were comparable to those reported with Ir-192 and were consistent with outcomes from other Co-60-based studies. Importantly, the longer half-life and reduced logistical demands of Co-60 make it particularly advantageous in low-resource environments where treatment interruptions due to source replacement can negatively impact outcomes.

6. Limitations of the Study

Several limitations must be acknowledged. First, the sample size was relatively small, limiting the generalizability of the findings. Second, patient attrition due to loss to follow-up may have influenced both toxicity and response assessments. The short follow-up period also precluded robust evaluation of long-term outcomes, including pelvic recurrence and distant metastasis. Additionally, other relevant toxicities, such as hematologic or dermatologic side effects, were not evaluated. Response assessment was performed only once, between 6–8 weeks post-treatment, and no correlation was made with detailed dosimetric parameters, which could have further enriched the analysis.

7. Conclusion

Our institutional experience with high-dose-rate intracavitary brachytherapy using a newly commissioned Cobalt-60 source for the treatment of cervical cancer has been encouraging. The

treatment yielded acceptable rates of both acute and late gastrointestinal and genitourinary toxicities, with clinical response rates that are both promising and comparable to those achieved with Iridium-192 in previous studies conducted at our centre. Notably, the late toxicity profile observed with Cobalt-60 was equivalent to that of Iridium-192, underscoring its clinical safety and effectiveness.

In addition to its comparable dosimetric characteristics, Cobalt-60 offers significant economic advantages due to its longer half-life, reducing the frequency and cost of source replacement by nearly half. This makes it a particularly attractive option for centres in resource-limited settings. While our short-term outcomes are favorable, long-term follow-up is necessary to draw definitive conclusions regarding survival, recurrence, and late toxicities.

Overall, HDR brachytherapy using a Cobalt-60 source represents a reliable, efficient, and cost-effective alternative to Iridium-192, and is increasingly being adopted globally as a preferred option for cervical cancer treatment in both high- and low-resource environments.

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Tables and Figures

Table I: Patient Characteristics

Patient Characteristics	
Characteristics	**Number (%) (n=52)**
Age Median	55 years (range 35- 71 years)
≤ 40 Year	05 (09.6)
41-50 Year	17 (32.7)
51-60 Year	20 (38.5)
61-70 Year	08 (15.4)
> 70 Year	02 (03.8)
Height Median	150 cm (range 139-161cm)
Weight Median	52.5 kg (30 kg-78 kg)
BMI Mean	23.7
Co-morbidities	
Yes	17 (32.7)
No	35 (67.3)
Addictions	
Yes	10 (19.2)
No	42 (80.8)
Parity	
< 4	20 (38.5)
≥ 4	32 (61.5)
Menstrual Status	
Pre-Menopausal	09 (17.3)
Post-Menopausal	43 (82.7)
Socioeconomic Status	
Lower (upper lower & lower)	30 (57.7)
Middle (upper & lower)	18 (34.6)
Upper	04 (07.7)
Place of Residence	
Rural	26 (50.0)
Urban	26 (50.0)
Karnofsky Performance Status	
60	0
70	0
80	26 (50.0)
90	26 (50.0)
Pre- Treatment Haemoglobin	
≤ 10	15 (28.8)
> 10	37 (71.2)

Table II: Tumor Characteristics

Tumor Characteristics	
CHARACTERISTICS	NUMBER (%) (n=52)
FIGO Staging (2018)	
IB (IB2 &IB3)	2 (3.8)
IIA	9 (17.3)
IIB	19 (36.5)
IIIA	4 (7.7)
IIIB	18 (34.6)
Grades of Differentiation	
Well Differentiated	8 (15.4)
Moderately Differentiated	35 (67.3)
Poorly Differentiated	9 (17.3)
Tumour Size	
≤ 4 cm	13 (25)
> 4 cm	39 (75)

Table III: Treatment Details

TREATMENT DETAILS	
DETAILS	Number (%) (n=52)
Duration between EBRT & ICRT	
≤ 2 Weeks	36 (69.2)
3-4 Weeks	16 (30.8)
Number of Concurrent Chemotherapies during EBRT	
< 5	18 (34.6)
5	34 (65.6)
Dosimetry	
Calculated mean dose to point-A	8.08 Gy/#
Calculated mean dose to bladder point	3.68 Gy/#
Calculated mean dose to rectal point	4.00 Gy/#

Table IV: Acute (A) & Late (B) Toxicities Assessment

A. ACUTE TOXICITY ASSESSMENT (n=52)		
TOXICITY/ GRADE	GRADE ≤1	GRADE ≥2
Upper Gastrointestinal	48 (92.3)	04 (07.7)
Lower Gastrointestinal	39 (75.0)	13 (25.0)
Genitourinary	49 (94.2)	03 (05.8)
B. LATE TOXICITY ASSESSMENT (n=45)		
TOXICITY/ GRADE	GRADE ≤1	GRADE ≥2
Gastrointestinal	40 (90.1)	05 (09.9)
Genitourinary	42 (93.3)	03 (06.7)

Table VI: Response Assessment

S.No.	Response	No. of Cases	(%)
1	Complete	38	84.4
2	Partial	5	11.1
3	Stable	0	0.0
4	Progressive	2	4.4
	Total	45	100.0

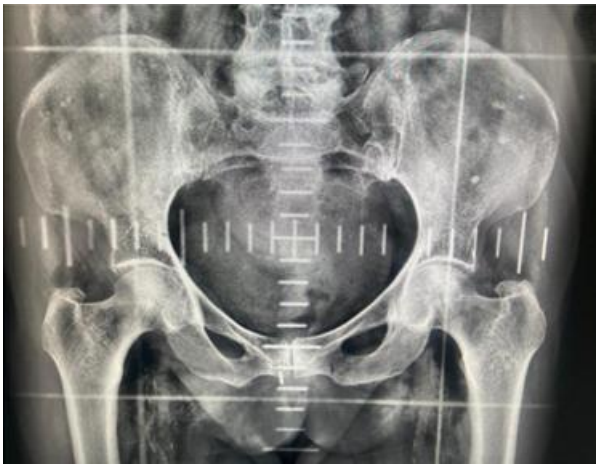

Figure 1: Simulation Film Showing Borders in AP- PA Filed for EBRT

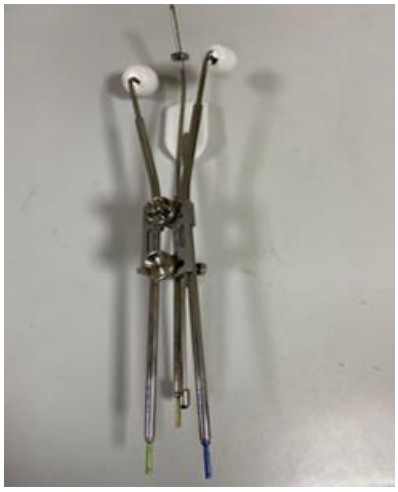

Figure 2: Fletcher Applicator with Tandem and Paired Ovoids

Figure 3: SAGINOVA by ECKERT & ZIEGLER BEBIG, Germany

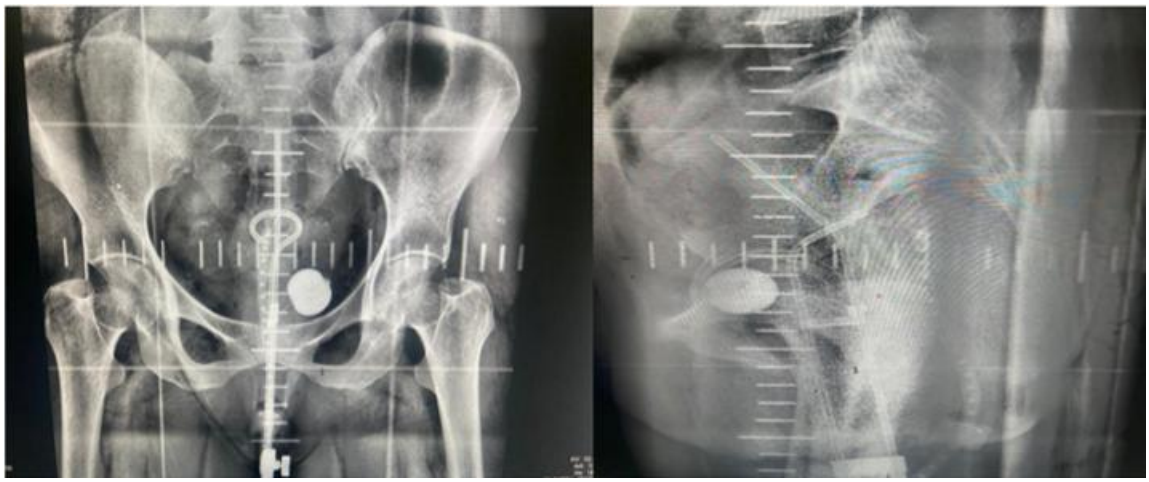

Figure 4 (a): AP and Lateral view of X- ray Simulation with Fletcher applicator with Tandem and Ring Applicator placed along with Foley's Catheter and Rectal Marker

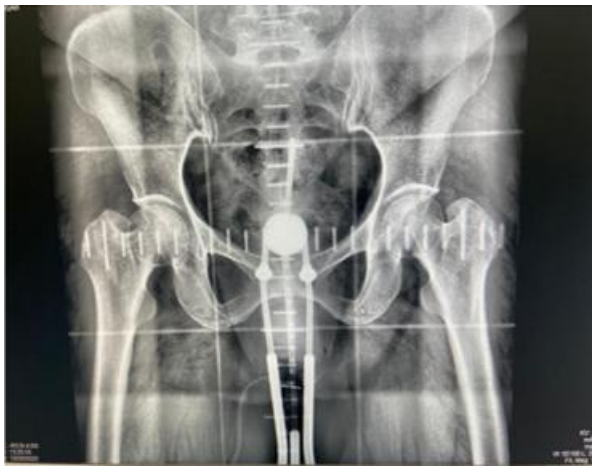

Figure 4 (b): AP view of X- Rays simulation with Fletcher Applicator with Tandem and Paired Ovoids

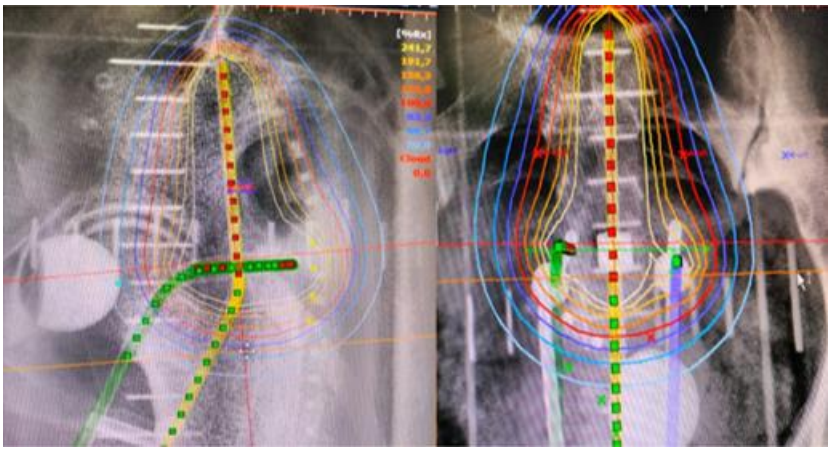

Figure 5: Orthogonal Radiographs showing Dwell positions and Isodose Distribution