



# Feasibility of Concurrent Chemoradiation in Cervical Cancer Patients From Rural Background

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## Abstract

**There is paucity of literature about tolerability of standard chemoradiation in cervical cancer patients of rural background; hence, we undertook this study. Enteritis and dyselektrolytemias were the most common toxicities and the key reasons for radiation interruption and suboptimal chemotherapy doses. Nutritional and social support along with vigorous assessment for dyselektrolytemias and timely management is the key to optimizing treatment.**

**Background:** Concurrent chemoradiation causes toxicities such as enteritis, hematologic toxicities which may lead to treatment interruptions, and therefore inferior outcomes. Adequate supportive care is very important to complete the scheduled protocol. Most of our patients are from rural background with a heterogeneous social background (nutrition and social support). There is paucity of literature to evaluate the tolerance of this intense treatment in these groups of patients, and hence, this study was undertaken. **Methods:** In this observational study, 30 rural women having carcinoma cervix treated with concurrent chemoradiation between January and July 2013 were reviewed retrospectively. They were assessed weekly for dyselektrolytemia, enteritis, and hematologic toxicity using Radiation Therapy Oncology Group Acute Radiation Morbidity Scoring Criteria. Treatment gaps along with reasons were recorded and correlated. **Results:** Median age of patients was 54 years. Of the patients, 43.3% were International Federation of Gynecology and Obstetrics stage II and 46.7% stage III. Grade 3 enteritis was seen in 7 of 30 patients (23.3%). None (0%) had grade 3 or higher hematologic toxicity. Dyselektrolytemia—hyponatremia (46.66%), hypokalemia (26.66%), hypocalcemia (6.66%), and hypomagnesemia (10%) were noted. Two of thirty patients (6.66%) received the planned 5 cycles, cisplatin 40 mg/m<sup>2</sup> weekly. There were treatment interruptions in radiation in 6 (20%) and treatment delays in chemotherapy in 10 (33.33%) patients. **Conclusion:** Concurrent chemoradiation for patients from rural areas is associated with higher acute toxicities. Regular monitoring for enteritis and dyselektrolytemias and timely intervention can help improve compliance and decrease treatment interruptions and thereby achieve the optimum treatment outcome.

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## Introduction

Cervical carcinoma is one of leading malignancies in Indian women with a higher burden as compared to western countries. In India, it accounts for 16% of all cancers in urban women and 37% of the cancers in rural women as published in 2009.<sup>1</sup> After National Cancer Institute alert (1999), the standard treatment is concurrent

chemoradiation using cisplatin as it has shown to reduce the risk of death by 30% to 50%.<sup>2</sup> Radiation therapy is delivered via teletherapy to a dose of 45 to 50 Gy followed by brachytherapy to a cumulative dose of 75 to 80 Gy to point A. This is combined with weekly 40 mg/m<sup>2</sup> cisplatin chemotherapy for 5 cycles.

Patients receiving chemoradiation have increased treatment-related toxicities as compared to radiation alone. These most commonly are nausea, enteritis, and hematologic toxicities. The odds ratios for grade 3 to 4 hematologic toxicities and grade 3 to 4 gastrointestinal (GI) toxicities in those who receive chemoradiation as against those treated with radiation alone are 8.97 and 2.77, respectively.<sup>3</sup> These toxicities cause treatment interruptions increasing overall treatment time and cumulative dose reduction of cisplatin. It compromises local control as prolongation of treatment beyond 56 days causes the local control to fall by 1% per day.<sup>4</sup>

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# Concurrent Chemoradiation in Rural Cervical Cancer

Adequate nutritional and supportive care is needed to manage side effects. These supportive parameters differ in different population backgrounds. Ours being a tertiary care set up with academic program, many patients from rural areas with compromised nutritional status receive treatment in our hospital. Of the patients with cervical cancer treated in our hospital between 1998 and 2005, 54.7% (140 of 257) were from rural background.<sup>5</sup> This study is attempted to assess the treatment compliance, enteritis, and hematologic toxicities in women of rural background treated with concurrent chemoradiation for cervical carcinoma. Rural background was particularly chosen as it constitutes over 60% of the Indian population, and the prevalence of cervical carcinoma is high in them. There is paucity of data regarding tolerance of standard chemoradiation in patients of rural background. Additional data will facilitate tailoring the treatment in the population.

## Material and Methods

### Patients

This is a retrospective study. Thirty patients of biopsy-proven cervical carcinoma (International Federation of Gynecologists and Oncologists [FIGO] stage IB to IVA) from rural background received treatment in our hospital between January and July 2013, and they were the subjects of our study. Their case files were reviewed. Demographic details were noted, and the diagnosis and stage were recorded according to the FIGO staging system.<sup>6</sup> Postoperative and palliative cases were excluded. Also, those patients with a history of inflammatory bowel disease or those who have medical comorbidities which deem them unfit for chemotherapy were excluded.

### Treatment

All patients were treated with radical intent, and none of them had received any prior oncology directed treatment. After obtaining written informed consent, external beam radiotherapy (EBRT) was delivered to a dose of 4500 cGy in 25 fractions using a 6-MV linear accelerator with SSD at 100 cm using 3-dimensional conformal radiation therapy. The volumes of interest were as per standard guidelines.<sup>7</sup> Cisplatin was planned to a dose of 40 mg/m<sup>2</sup> concurrently with EBRT for 5 cycles. All patients were treated as inpatients during concurrent chemoradiation. Minimum of 10 gm/dL hemoglobin was maintained at the beginning of treatment. After a gap of 2 weeks, intracavitary brachytherapy was done under combined spinal/epidural anesthesia using manual after-loading low-dose-rate cesium sources. The planning was done by digitizing the sources on orthogonal x-rays and a dose of 30 Gy was prescribed to point A.

### Toxicity Assessment During EBRT

Weekly blood counts (complete hemogram), renal function tests, and serum electrolytes were measured. The number of episodes of loose stools and vomiting was documented. Abnormalities in blood parameters and degree of enteritis were graded as per Radiation Therapy Oncology Group (RTOG) Acute Radiation Morbidity Scoring Criteria<sup>8</sup> (described in the following) and accordingly treated. Implications of these toxicities in terms of treatment interruptions were recorded and correlated.

#### *RTOG Acute Radiation Morbidity Scoring Criteria.*

Grade 0: indicates no change in bowel habit.

Grade 1: increased frequency or change in quality of bowel habits not requiring medication or rectal discomfort not requiring analgesics.

Grade 2: diarrhea requiring parasympatholytic drugs (eg, Lomotil)/mucous discharge not necessitating sanitary pads/rectal or abdominal pain requiring analgesics.

Grade 3: diarrhea requiring parenteral support/severe mucous or blood discharge necessitating sanitary pads/abdominal distention. (Flat-plate radiograph demonstrates distended bowel loops.)

Grade 4: acute or subacute obstruction, fistula, or perforation; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion.

## Results

Total patients reviewed were 30. The Karnofsky performance score for all patients ranged from 80 to 90.

### Study Population

Patients' age ranged from 30 to 75 years with a mean of 52.53 years and median of 54 years. Thirteen patients (43.33%) were ≤ 50 years and 17 (56.66%) were > 50 years. Most patients belonged to FIGO stages II and III. The stage-wise distribution of the patients is presented in Table 1. All patients had squamous cell carcinoma.

### Toxicities

Patients were assessed for acute toxicities encountered during radiation therapy. Weekly scoring of radiation enteritis as per RTOG scoring criteria revealed maximum enteritis scores for each patient as presented in Table 2. Of the patients, 76.66% had grade I to II toxicities, whereas 23.33% had grade III toxicities.

The changes encountered in parameters of hemogram pertaining to hemoglobin, total leukocyte count, and absolute neutrophil count are provided in Table 3. There was no significant drop in platelet count in any of the subjects of our study. Serum creatinine also remained normal throughout the study for all patients. Figure 1 shows a graph of percentage of patients who had dyselektrolytemia during the treatment course. Decrease in serum sodium was the most frequent abnormality (14 of 30) followed by potassium (8 of 30).

### Treatment Gaps During Radiation Therapy

Six patients (20%) required gap during radiation therapy. The gap ranged from 3 to 10 days. The reasons were 3 patients had grade 3 enteritis, 1 had dyselektrolytemia, 1 had severe pain abdomen, and 1 had both grade 3 enteritis and dyselektrolytemia.

**Table 1** Showing Stage-Wise Distribution of Patients

Stage (FIGO)	Number of Patients (%)
Stage I	2 (6.66)
Stage II	13 (43.33)
Stage III	14 (46.66)
Stage IVA	1 (3.33)

Abbreviation: FIGO = Fédération Internationale de Gynécologie et d'Obstétrique.

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