Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/251

Original Article

A Prospective Analysis of Toxicities and Quality of Life after Treatment in Advanced Carcinoma Cervix Patients Following Concurrent Chemoradiation with Weekly Cisplatin

Jayaraman Balan[1], T S Sudhiraj[2], Deepak George[3], Jewell Joseph[3], R Mahadevan[4]

[1]Associate Professor, Department of Radiotherapy and Oncology, Government Medical College, Thrissur, Kerala, India, [2]Assistant Professor, Department of Community Medicine, Government Medical College, Thrissur, Kerala, India, [3]Senior Resident, Department of Radiotherapy and Oncology, Government Medical College, Thrissur, Kerala, India, [4]Professor, Department of Radiotherapy, Government Medical College, Thiruvananthapuram, Kerala, India

Abstract

Introduction: Cervical cancer is the most frequently diagnosed cancer among women in India. Understanding quality of life (QOL) in women undergoing Chemoradiotherapy for cervical cancer will help in introducing interventions for better care and outcomes in these women.

Aim: To study toxicities and quality of life after treatment in advanced carcinoma cervix patients following concurrent chemoradiation with weekly cisplatin

Patients and Methods: Newly diagnosed patients with histologically confirmed carcinoma cervix, Patients with FIGO STAGE IIB TO IVA and no evidence of distant metastasis. Gynecological Oncologic group performance status of 0-3, Age less than 70 years, WBC count greater than 4000 cells/ml, An absolute neutrophil count greater than 37.5%, Platelet count of 100000 platelets/ml, Serum creatinine < 1.5mg/dl, Creatinine clearance more than 80 ml/min, Hemoglobin value >8 gm%. The patient treated with concurrent chemoradiation with weekly cisplatin

Results: Out of the 45 patients only 6 patients developed grade 3 neutropenia (13.3%), 12 patients (26.7%) developed grade 2 neutropenia, and there were no incidences of grade 4 neutropenia, during radiation, 4(8.9%) patients developed grade 3 skin reaction and 3(6.7%) patients developed grade 1 skin reaction. The quality of life decreased during treatment.

Conclusion: The patients who underwent chemoradiation experienced the reduction in quality of life during the treatment, but it was transient. The symptoms subsided and after the treatment patients have a better quality of life compared to pretreatment status. the toxicities of the treatment can be managed conservatively., which is comparable with global standards

Key words: Pelvic radiation toxicity, Quality of life, Cisplatin, Cervical cancer, Concurrent chemo radiotherapy

INTRODUCTION

Cervical cancer is the second most common cancer in women worldwide and the major cause of death, particularly in the developing countries.[1] The global yearly incidence of cervical cancer in 2012 was 528,000; the annual death rate was 26600.[2] The incidence of cervical cancer per 1 lakh women in India is 30.7. The highest rate of incidence is seen in Latin American women. Poor nutritional status, multiple sexual partners, first coitus in young age, early childbirth, promiscuity of the spouse, HPV infections, sexually transmitted diseases, and immunocompromised states are cited as main risk factors.[3] Introduction of cervical screening tests reduces the incidence of invasive cervical cancer in the Western world. In developing or less developed countries, over

Access this article online

www.ijss-sn.com

Month of Submission : 07-2018
Month of Peer Review : 08-2018
Month of Acceptance : 09-2018
Month of Publishing : 09-2018

Corresponding Author: Dr. T S Sudhiraj, Department of Community Medicine, Government Medical College,Thrissur, Kerala, India.
E-mail: drsudhiraj@gmail.com

80% of women with cervical cancer are diagnosed at the advanced stage which is associated with poor prognosis.[4] Radiation therapy (RT) alone was being used as a primary treatment for patients with locally advanced - the International Federation of Gynecology and Obstetrics (FIGO)[5] Stage IIB to IV - cervical cancer, but failure rates were high, suggesting the need of additional therapeutic modalities.[6] Many randomized studies suggest that a combination of chemotherapy with radiation will increase the effect of radiation.[7] Prognosis depends on the initial disease stage (FIGO), tumor volume, nodal status, radiation dose, treatment duration, hemoglobin level, and optimum use of intracavitary brachytherapy.[8] There are many randomized studies which incorporate chemo with radiation; in the 1980s, result of these studies shows that concurrent chemoradiation lowers the risk of recurrence and death.[9,10] The most common histological type is squamous cell carcinoma comprising around 80%.

Aim

The aim is to study the toxicities and quality of life (QOL) after treatment in patients with locally advanced carcinoma cervix.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of Radiotherapy, Government Medical College, Thrissur.

Inclusion Criteria

Newly diagnosed patients with histologically confirmed carcinoma cervix, patients with FIGO Stage IIB to IVA, and patients with no evidence of distant metastasis, Eastern Cooperative Oncology Group(ECOG) performance status of 0–3, age <70 years, white blood cell (WBC) count >4000 cells/ml, an absolute neutrophil count >37.5%, platelet count of 100000 platelets/ml, serum creatinine <1.5 mg/dl, creatinine clearance >80 ml/min, and hemoglobin value >8 g% were included in the study.

Exclusion Criteria

The following criteria were excluded from the study: Carcinoma cervix FIGO Stage IA-IIA, history of renal disease, coronary artery diseases, uncontrolled hypertension, presence of distant metastasis, age >70 years, WBC count <4000 cells/ml, an absolute neutrophil count <37.5%, platelet count <100000 cells/ml, serum creatinine >1.5, creatinine clearance <80 ml/min, and hemoglobin value <8 g%.

A thorough clinical examination was performed including per-speculum examination, per vaginal examination, digital rectal examination, and per-abdominal examination. In all patients, investigations such as chest X-ray, ultrasonography abdomen, magnetic resonance imaging, complete blood count, renal function test, liver function test, urinalysis, cystoscopy, and sigmoidoscopy were performed only in patients clinically suspicious of bowel and bladder invasion.

All patients were monitored closely weekly during concurrent chemoradiation for assessing the toxicity of therapy. Toxicity grading was done according to the RT oncology group grading. The patients require to follow up at 6 weeks from completion of therapy to assess response, toxicity, and disease status. Subsequent follow-up visits were scheduled at monthly. At follow-up, patients underwent a thorough clinical examination for detection of locoregional disease. Patients who drop out or do not complete the planned course of treatment will be excluded.

RESULTS

Mean age of the study population was 57 years, ranging from 35 to 70 years. Majority of patients (20, 44.1%) are in the age group of 61–70 years old. 11 patients (24.1%) are below the age of 50 years, and 14 patients (31.1%) are the age group of 51–60 years. Bleeding PV and discharge PV were present in 38 (84.4%) patients, and pain was present in 25 (55.6%) of patients. 22 (48.9%) patients of 45 have ECOG 0 and 23 (51.1%) patients have ECOG 1. 20 (44.4%) patients have vaginal involvement; 25 (55.6%) patients do not have vaginal involvement. 21 (46.7%) patient have 4-cm size lesion, 13 (28.9%) have 5-cm lesion, 5 (11.1%) have 6-cm lesion, 3 (6.7%) have 3-cm lesion, 2 (4.4%) have 5.5-cm lesion, and 1 (2.2%) has 2.8-cm lesion. 7 (15.6%) have adjacent structure involvement; 38 (84.4%) patients do not have adjacent structure involvement. 26 (57.8%) patients have initial stage of 2B, 13 (28.9%) have 3B, 5 (11.1%) have 4A, and only 1 (2.2%) have 3A stage. 35 (77.8%) patients received only 4 cycles of concurrent chemotherapy and 10 (22.2%) received 5 cycles of concurrent chemotherapy. 21 (46.7%) developed Grade 2 neutropenia, 12 (26.7%) developed Grade 1 neutropenia, 6 (13.3%) developed Grade 0 neutropenia, and 6 (13.3%) developed Grade 3 neutropenia. 21 (46.7%) developed Grade 1 cystitis during RT and 24 (53.3%) developed Grade 2 cystitis. 21 (46.7%) patients developed Grade 2 nausea, 22 (48.9%) developed Grade 1, and 2 (4.4%) developed Grade 0 reaction. 18 (40%) have Grade 1 diarrhea and 27 (60%) developed Grade 2 diarrhea during radiation. 38 (84.4%) patients developed Grade 2 skin reaction during radiation, 4 (8.9%) developed Grade 3 skin reaction, and 3 (6.7%) developed Grade 1 skin reaction.

QOL Analysis

Repeated measures ANOVA was carried out for comparing pre-treatment, during treatment, and after treatment parameters of QOL.

F-value (137.202) was found to be significant, indicating that there exists the significant difference in the CXBI (body image scale) measured at 3 times. During the treatment, a significant decrease was noted, and it increased in the after treatment period. *P*-value of the comparison between pre-treatment and after treatment value (<0.0001) indicates that there exists significant difference. Mean value before the treatment is 54.3 and it increases to 60.0 after the treatment ($P < 0.0001$).

In the case of sexual activity, during the treatment, a significant increase is noted followed by a significant decrease. *P*-value of the comparison between pre-treatment and after treatment (0.323) indicates that there is no significant difference between sexual activity before and after the treatment. The mean value is 71.1, 100, and 73.3 before, during, and after the treatment, respectively (F-value = 45.150).

During the treatment, there are a significant increase in symptom experience and a significant decrease thereafter. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there is a significant decrease in symptoms after the treatment. The mean values are 48.89, 60.34, and 44.58 before, during, and after the treatment, respectively (F-value = 145.438).

During the treatment, there are a significant increase in lymphedema and a significant decrease thereafter. *P*-value of the comparison between pre-treatment and after treatment (0.013) indicates that there is a significant increase in lymphedema. The mean value is 0.74, 13.33, and 5.9 before, during, and after the treatment, respectively (F-value = 15.525).

During the treatment, there are a significant increase in peripheral neuropathy and a significant decrease thereafter. *P*-value of the comparison between pre- and post-treatment (0.002) indicates that there is a significant increase in the peripheral neuropathy. The mean values are 0, 8.15, and 6.67 before, during, and after the treatment, respectively (F-value = 9.402).

During the treatment, there is a significant increase in menopausal symptoms, and after the treatment, there is no change in the menopausal symptoms. The mean values are 42.96, 46.67, and 46.67, respectively, before, during, and after the treatment (F-value = 1.583).

During the treatment, there is a significant increase in sexual worry followed by a significant decrease in post-treatment. There is no significant difference in sexual worry before and after the treatment ($P = 0.051$). The mean values are 28.59, 54.81, and 23.70, respectively, before, during, and after the treatment (F-value = 39.878) [Figures 1-4].

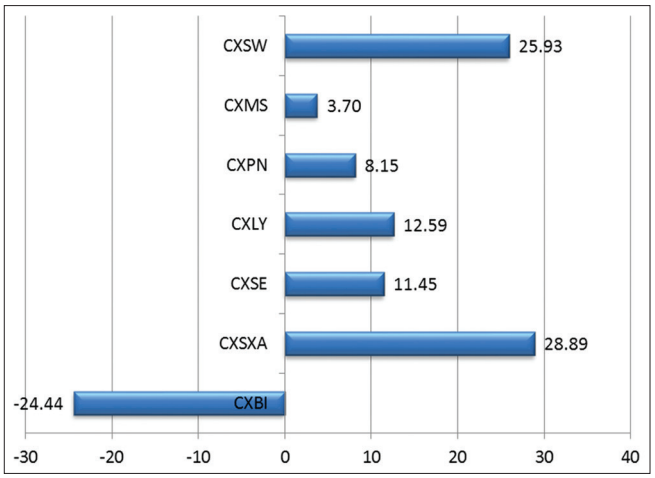

Figure 1: Difference in mean quality of life during radiation therapy (RT) and before RT. CXSW - Sexual worry, CXMS - Menopausal symptoms, CXPN - Peripheral neuropathy, CXLY - Lymphedema, CXSE - Symptom experience, CXSXA - Sexual activity, CXBI - Body image

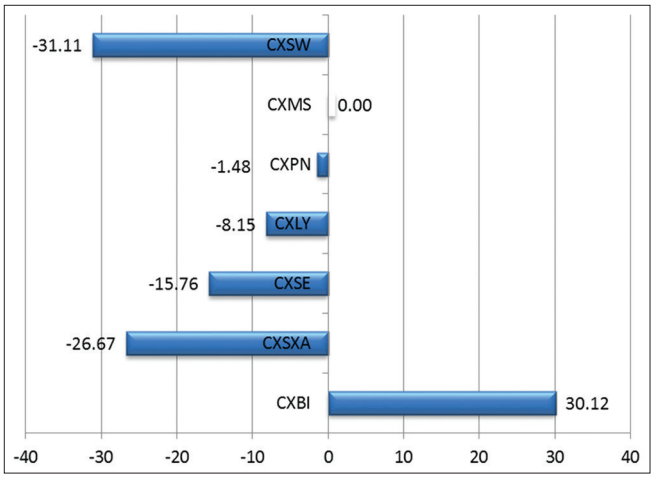

Figure 2: Difference in mean quality of life after radiation therapy (RT) and during RT. CXSW - Sexual worry, CXMS - Menopausal symptoms, CXPN - Peripheral neuropathy, CXLY -Lymphedema, CXSE - Symptom experience, CXSXA - Sexual activity, CXBI - Body image

During the treatment, there is a significant decrease in global health status followed by a significant increase. *P*-value of the comparison between pre- and post-treatment is <0.001, indicating that there is a significant increase in global health status after the treatment. Mean values are 42.04, 28.70, and 52.22, respectively, before, during, and after the treatment.

During the treatment, there is a significant decrease in physical functioning, with a significant increase in post-treatment. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there is a significant improvement in the physical functioning after the treatment, and the mean values are 68.44, 57.33, and 74.67, respectively, before, during, and after the treatment.

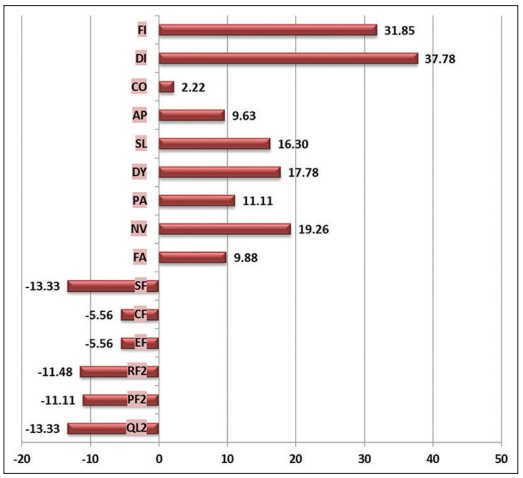

Figure 3: Difference in mean quality of life during radiation therapy (RT) and before RT. QL2 - Global health status, PF2 - Physical functioning, RF2 - Role of functioning, EF - Emotional functioning, CF - Cognitive functioning, SF - Social functioning, FA - Fatigue, NV - Nausea and vomiting, PA - Pain, DY - Dyspnea, CO - Constipation, SL - Insomnia, AP - Appetite, DI - Diarrhea, FI - Financial difficulties

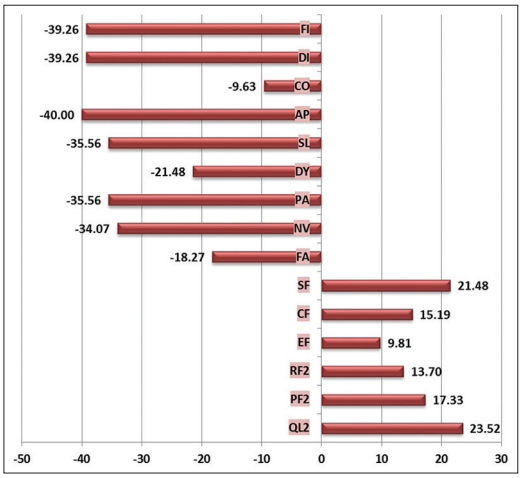

Figure 4: Difference in mean quality of life after radiation therapy (RT) and during RT. QL2 - Global health status, PF2 - Physical functioning, RF2 - Role of functioning, EF - Emotional functioning, CF - Cognitive functioning, SF - Social functioning, FA – Fatigue, NV - Nausea and vomiting, PA - Pain, DY - Dyspnea, CO - Constipation, SL - Insomnia, AP - Appetite, DI - Diarrhea, FI - Financial difficulties

During the treatment, there is a significant decrease in the role of functioning, after that there is a significant increase. *P*-value of the comparison between pre- and post-treatment (0.294) indicates that there is no significant difference between the roles of functioning after the treatment, and the mean values are 41.85, 30.37, and 44.07, respectively, before, during, and after the treatment (F-value = 19.702).

During the treatment, there was a significant decrease in the emotional functioning, with a significant increase after treatment. *P*-value of the comparison between pre-treatment and after treatment (<0.001) indicates that there is a significant increase in emotional functioning after the treatment, and the mean values are 60.93, 55.37, and 65.19, respectively, before, during, and after the treatment (F-value = 31.435).

During the treatment, there were a significant decrease in the cognitive functioning and a significant increase afterward. *P*-value of the comparison between pre- and post-treatment (0.001) indicates that there is a significant improvement in the cognitive function after the treatment, and the mean values are 46.67, 41.11, and 56.30, respectively, before, during, and after the treatment (F-value = 34.764).

During the treatment, the social functioning score shows a significant decrease after that there is a significant increase. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there is a significant increase in social functioning score after the treatment, and the mean values are 57.04, 43.70, and 65.19, respectively, before, during, and after the treatment (F-value = 43.00).

During the treatment, there was a significant increase in fatigue, with a decrease after treatment. *P*-value of the comparison between pre-treatment and after treatment (<0.001) indicates that there is a significant decrease in fatigue after the treatment, and the mean values are 49.38, 59.26, and 40.99, respectively, before, during, and after the treatment (F-value = 81.249).

During the treatment, there was a significant increase in nausea and vomiting, with a significant decrease after treatment. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there was a significant decrease in nausea and vomiting after the treatment, and the mean values are 43.33, 62.59, and 28.52, respectively, before, during, and after the treatment (F-value = 115.310).

During the treatment, there was a significant increase in pain with a significant decrease in pain after treatment. *P*-value of the comparison between pre-treatment and after treatment (<0.001) indicates that there was a significant decrease in pain, and the mean values are 57.04, 68.15, and 32.59, respectively, before, during, and after the treatment (F-value = 113.749).

During the treatment, there were a significant increase in dyspnea and a significant decrease in dyspnea after treatment. *P*-value of the comparison between pre- and post-treatment (0.024) indicates that there was a significant decrease in dyspnea after the treatment, and the mean value are 27.41, 45.19, and 23.70, respectively, before, during, and after the treatment (F-value = 47.068).

There was no significant increase in constipation during treatment. *P*-value of the comparison between pre- and post-treatment (0.017) indicates that there was a significant decrease in constipation after the treatment, and the mean values are 20, 22.22, and 12.59, respectively, before, during, and after the treatment (F-value = 6.499).

During the treatment, there was a significant increase in insomnia followed by a significant decrease after treatment. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there was a significant decrease in insomnia after the treatment; the mean values are 45.19, 61.48, and 25.93, respectively, before, during, and after the treatment (F-value = 66.383).

During the treatment, there was significant appetite loss with a significant improvement in appetite post-treatment. *P*-value of the comparison between pre- and post-treatment (<0.001) indicates that there was a significant improvement in appetite after treatment; the mean values are 49.63, 59.26, and 19.26, respectively, before, during, and after the treatment (F-value = 43.00).

During the treatment, there was a significant increase in diarrhea, and after the treatment, there was a significant reduction in diarrhea. *P*-value of the comparison between pre-treatment and after treatment (0.623) indicates that there was no significant decrease in diarrhea after the treatment; the mean values are 12.59, 50.37, and 11.11, respectively, before, during, and after the treatment (F-value = 43.00).

During the treatment, there was a significant increase in financial difficulties, and after the treatment, there was a significant decrease in financial difficulties. *P*-value of the comparison between pre- and post-treatment (0.006) indicates that there was a significant decrease in financial difficulties after the treatment, and the mean values are 25.93, 57.78, and 18.52, respectively, before, during, and after the treatment (F value = 43.00).

DISCUSSION

QOL assessment reveals that there are an increase in the body image score and a decrease in the symptom score after treatment. There was an increase in lymphedema after the treatment, which may be attributed to radiation. There was also an increase in peripheral neuropathy after the treatment which may be due to the concurrent use of cisplatin. There were no significant changes in menopausal symptoms, sexual worry, and sexual activity when compared to the pre-treatment status. Aggravation of symptoms was observed during the treatment. The global health status, physical functioning, emotional functioning, cognitive functioning, and social functioning decreased during treatment but significantly improved after treatment. Fatigue, nausea, vomiting, pain, insomnia, diarrhea, and financial difficulties increased during treatment but significantly reduced after treatment. There was no significant change in the occurrence of diarrhea compared to the pre-treatment status.

Monitoring the QOL in disease-free period after radiotherapy should include the information about the treatment complications since it might help the patients deal with them and cure the disease symptoms. It is important to monitor the mental status of cervical cancer patients in the assessment of their QOL. While some studies indicate a low mental status with irradiated patients, this study reveals significant improvements of emotional functions, higher role function, and better social integration, which significantly affect a mental status. Due to tumor regression, pain and fatigue were significantly reduced in patients after the irradiation.[11-13]

CONCLUSION

The patients who underwent chemoradiation experienced reduction in QOL during the treatment, but it was transient. The symptoms subsided, and after the treatment, patients had better QOL compared to pre-treatment status.

REFERENCES

1. Kong TW, Chang SJ, Paek J, Yoo SC, Yoon JH, Chang KH, *et al.* Comparison of concurrent chemoradiation therapy with weekly cisplatin versus monthly fluorouracil plus cisplatin in FIGO stage IIB-IVA cervical cancer. J Gynecol Oncol 2012;23:235-41.
2. International Agency for Research on Cancer. Cervical Cancer Estimated Incidence, Mortality and Prevelance Worldwide in 2012. Geneva: World Health Organization; 2012.
3. Narayanan V, Bista B, Sharma S. External beam therapy in a four-field box technique with paclitaxel versus a two-field technique with cisplatin in locally advanced carcinoma cervix: A Phase II monocentric trial. ISRN Oncol 2012;2012:390193.
4. Denny L. Cervical cancer treatment in Africa. Curr Opin Oncol 2011;23:469-74.
5. Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC Cancer Staging Manual. 7th ed. New York: Springer; 2010.
6. Jampolis S, Andras EJ, Fletcher GH. Analysis of sites and causes of failures of irradiation in invasive squamous cell carcinoma of the intact uterine cervix. Radiology 1975;115:681-5.
7. Byfield JE, Calabro-Jones P, Klisak I, Kulhanian F. Pharmacologic requirements for obtaining sensitization of human tumor cells *in vitro* to combined 5-fluorouracil or ftorafur and X rays. Int J Radiat Oncol Biol Phys 1982;8:1923-33.
8. Geara FB, Shamseddine A, Khalil A, Abboud M, Charafeddine M, Seoud M. A phase II randomized trial comparing radiotherapy with concurrent weekly cisplatin or weekly paclitaxel in patients with advanced cervical cancer. RadiatOncol2 010 Sep 23;5:84.
9. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler WC Jr, *et al.* Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: A Gynecologic oncology group and Southwest oncology group study. J Clin

Oncol 1999;17:1339-48.
10. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, *et al.* Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med 1999;340:1137-43.
11. Kragelj B. Increased late urinary toxicity with whole pelvic radiotherapy after prostatectomy. Radiol Oncol 2009;43:88-96.
12. Klee M, Thranov I, Machin Prof D. The patients' perspective on physical symptoms after radiotherapy for cervical cancer. Gynecol Oncol 2000;76:14-23.
13. Korfage IJ, Essink-Bot ML, Mols F, van de Poll-Franse L, Kruitwagen R, van Ballegooijen M, *et al.* Health-related quality of life in cervical cancer survivors: A population-based survey. Int J Radiat Oncol Biol Phys 2009;73:1501-9.

How to cite this article: Balan J, Sudhiraj TS, George D, Joseph J, Mahadevan R. A Prospective Analysis of Toxicities and Quality of Life after Treatment in Advanced Carcinoma Cervix Patients Following Concurrent Chemoradiation with Weekly Cisplatin. Int J Sci Stud 2018;6(6):64-69.

Source of Support: Nil, **Conflict of Interest:** None declared.