



Review article

Challenges to cervical cancer treatment in Bangladesh: The development of a women's cancer ward at Dhaka Medical College Hospital



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ABSTRACT

Cervical cancer is the second most common cause of female cancer mortality worldwide. Concurrent chemoradiotherapy represents the standard of care for patients with stages IB2 to IVa cervical cancer. Unfortunately radiation therapy capacity is severely limited to non-existent in many Low and Middle-Income Countries. One solution has been to use chemotherapy to reduce tumor size to allow for radical surgery or in the case of inoperable cancers, as a placeholder until radiation is available. In Bangladesh, there has been the progressive development of resources for the treatment of women with gynecologic cancers. However, radiation therapy resources are limited with a six-month waiting period to receive radiation. Neoadjuvant chemotherapy (NACT) remains the main primary treatment intervention for women with advanced cervical cancer in Bangladesh. This implementation study summarizes of the experience and challenges to caring for women in a new gynae-oncology ward at Dhaka Medical College Hospital, a 2600 bed government hospital in Dhaka, Bangladesh.

1. Introduction

Cancer is a global problem accounting for almost 13% of all deaths worldwide. This equates to over seven million people a year, more than is caused by HIV/AIDS, TB and malaria combined (Sharma et al., 2011). Cervical cancer is the fourth most frequent cancer among women worldwide and the most frequent cancer among women in Africa, Asia, and South America with an estimated incidence of 528,000 per year with 266,000 annual cervical cancer deaths (Globocan, 2012). Although there is effective screening for cervical cancer, it continues to be a healthcare problem in developing countries where effective screening programs are limited (Saslow et al., 2012; Denny et al., 2017).

Cervical cancer is the second leading malignancy, in terms of both incidence and mortality, among Bangladeshi women (Globocan, 2012). While incidence and treatment modalities for cervical cancer have been previously investigated in Bangladeshi populations (Hussain, 2013), there is virtually no published information regarding outcomes among those treated from cervical cancer. There are significant challenges to the development of infrastructure for cancer care in Bangladesh. Data collection in resource-limited countries has been challenging and new options using low-tech applications have been suggested (Perosky et al., 2015). Additionally there is a limited physical infrastructure and

deficient resources to treat cancer such as an inadequate number of radiotherapy units.

The opportunities for cancer care for women in Bangladesh will depend on their socioeconomic status. With a total country population of 162,910,864 and 18.5% of the population making < 1.9 USD per day, many Bangladeshis will receive care through government sponsored hospitals and health centers (Worldometer, 2017; World Bank, 2017).

While nationwide, there are approximately twenty hospitals that offer cancer care, most oncology referrals are directed to public hospitals. The Dhaka Medical College Hospital is overwhelmed by the influx of patients, which greatly outstrips the number of inpatient beds. The 300 bed National Institute for Cancer Research Hospital (NICRH) has an annual turnover of 15,000 to 20,000 cancer patients, and Bangabandhu Sheikh Mujib Medical University (BSMMU) 5000–6000 cancer patients. However the number of trained oncologists is inadequate for the volume of patients. Dhaka Medical College and Hospital (DMCH) is a medical college and hospital located in Dhaka, the capital city of Bangladesh (Dhaka Medical College Hospital, 2017). Since its creation in 1946, DMCH has served as the largest public hospital in Bangladesh. With the motto “no patient turned away”, DMCH admits and treats the poorest patients from all over Bangladesh.

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While the hospital has 2600 beds, an average daily census is 3000 to 3500 patients as patients are doubled up in beds, lie on the floor on mats in the wards, the hospital hallways, and the stairwells. Fifteen percent of patients are able to pay for medical care and the remainder receives free care. In 2015, a small gynae-oncology unit was created at DMCH. This review reports on the recent experience with the development of a women's cancer program at DMCH.

2. Materials and methods

The literature on chemotherapy and radiation for women with inoperable cervical cancer in LMIC was reviewed. Data from Bangladesh was abstracted from Globcan, World Bank, and current literature from Bangladesh (Globcan, 2012; Hussain, 2013; Hussain and Sullivan, 2013; World Bank, 2017). The experience of the treatment of women with cervical cancer at DMCH was abstracted from the recent written tumor board notes from the department of obstetrics and gynecology.

3. Women's services at Dhaka Medical College Hospital

The facilities for the care of women patients includes a large ward for obstetrical patients, a second large ward for gynecologic and post-operative patients, a ward devoted to the care of women with pre-eclampsia and eclampsia, another ward for the care of women with obstetrical fistulas, and a new gynae oncology unit. There are no sinks or garbage facilities in the wards (Shahida et al., 2016). This structural lack is associated with hospital-acquired infection rates exceeding 30% (Weinshel et al., 2015). There is a daily average of 75 admissions to the department of Obstetrics and Gynecology at DMCH. A total of 339 beds are reserved for obstetric and gynecology patients. Table 1 shows the breakdown facilities and daily patient census.

The Gynae oncology ward opened in 2015 and has been at capacity since the beginning (Fig. 1).

Table 2 summarizes the total gynecologic oncologic admissions for 2015. Women with cervical cancer accounted for 19% of ward admissions. Forty-eight (38%) of these patients underwent Wertheim radical hysterectomies for cancers varying from stage Ib2 to IIb. Patients with bulky stage IIb cancers received NACT prior to surgery. The average wait for radiation therapy at DMCH is over six months. As a result, the most common management strategy for large cervical cancers is to administer chemotherapy with the hope of shrinking the cancer enough to allow a surgical resection. Patients with unresectable disease were referred for carboplatin and paclitaxel neoadjuvant chemotherapy followed by concurrent weekly cisplatin chemotherapy and external beam radiotherapy. Figs. 2 and 3 show the radiotherapy department at DMCH. In particular, 79 patients (62%) were treated with neoadjuvant chemotherapy. As these patients came from villages that took more than a day to travel to, the majority remained in hospital for chemotherapy administration. Patients who could return for outpatient

Table 1

Type of available hospital wards for Obstetrics and Gynecology at Dhaka Medical College Hospital and average daily patient statistics.

Hospital ward type	Number of patients in each ward
Obstetrics	177
Gynecology	142
Gynae oncology ward	25
Subfertility	5
Vesicovaginal fistula	43
Infection ward	10
General ward	49
Private room (cabins)	147
Total patients ^a	598
Total beds	319

^a There are more patients than available beds leading to doubling up of patients per hospital bed.



Fig. 1. Gynae Oncology Ward at Dhaka Medical College Hospital.

Table 2

Number of women admitted to the Gynae Oncology Ward in 2015 at Dhaka Medical College Hospital.

Diagnosis	Number of patients
Cervical cancer	127
Ovarian cancer	320
Persistent gestational trophoblastic disease	197
Endometrial cancer	2
Vulvar cancer	12
Total	658

chemotherapy, received their chemotherapy in the six bed outpatient chemotherapy unit (Fig. 4). Chemotherapy regimens included various combinations including a platinum drug (see Table 3).

Follow-up and survival rates for the majority of these patients are unknown. There is no current capacity and infrastructure to track patients. The majority of the patients either come from rural villages or are slum dwellers with no fixed address in Dhaka.

4. Discussion

The success to creating a complex, multidisciplinary program to treat life-threatening cancers depends on multiple factors from the individual to societal. There are challenges and barriers to the development of such programs in resource limited countries. Primary Barriers are the immediate challenges that a physician may face to provide care. These may include: personal training limitations, lack of support staff, lack of equipment and supplies to allow ideal care. Secondary barriers are the surrounding environmental challenges within which a physician is placed such as the inability to travel due to traffic, political turmoil and strikes, the built environment of the hospital such as lack of sinks, garbage disposal, and poverty of the patient population that does not allow them to access care. This paper describes the development of a small women's cancer ward in the largest hospital in Bangladesh, Dhaka Medical College Hospital (DMCH). There are tremendous barriers to care for women with newly diagnosed cervical cancers, the leading gynecologic cancer in Bangladesh. In Bangladesh, 80% women present with advanced stage (Stage III–IV) cervical cancer, which is invariably fatal in this country (Hussain and Sullivan, 2013). Huge numbers of patients have to wait for radiotherapy, a scarce and limited resource. Invariably, the majority of these women do not receive care and die from the natural history of untreated cervical cancer. A growing strategy has been the use of neoadjuvant chemotherapy to either render



Fig. 2. Entry to the Radiotherapy Department, Dhaka Medical College Hospital.

the cancer surgically resectable or as a delaying tactic while waiting for radiation. A significant barrier to comprehensive care is the current lack of data on short and long term outcomes for these women.

5. Radiation therapy in Bangladesh

Worldwide, < 35% of the radiation facilities reside in Low and Middle Income Countries (LMICs) (IAEA, 2011). At least one radiotherapy unit for every 250,000 people is available in most high income countries; while, a survey of twenty low and middle income countries found that one radiotherapy unit to every five million people and sometimes, one unit for every 20 million people is available (Grover et al., 2015). Currently, 30 countries (15 in Africa and Asia) do not have any radiation machine (Zubizarreta et al., 2015).

In Bangladesh there are ten government medical college hospitals and four private-pay hospitals (Delta Oncology Center, United Hospital, Khwaja Yunus Ali Medical College Hospital and Square hospital) with radiation facilities (Uddin et al., 2013). National Institute of Cancer Research Hospital (NICRH), a 150 bed government cancer hospital in Dhaka, is best equipped government hospital with three dual-energy linear accelerators and two cobalt 60 machines, and high-dose-rate (HDR) brachytherapy. DMCH has one cobalt machine and one linear accelerator and high-dose rate brachytherapy. Radiation therapy and Brachytherapy has been inconsistent at DMCH due to equipment maintenance problems. In 2015 Bangladesh had 13 Linear Accelerators, 12 Cobalt 60 machines and 6 high-dose rate Brachytherapy machines in

15 centers (Atun et al., 2015).

Only 11.2% patients get access to Radiation therapy treatment because of this shortage, specifically, there are a total of 151 Tele-therapy units, 282 Radiation oncologists, 165 medical physicists and 487 radiation therapy technologists in Bangladesh (Datta et al., 2014). Because of the critical shortage of radiotherapy, primary chemotherapy for advanced cervical cancer is normative in Bangladesh.

6. Neoadjuvant chemotherapy for cervical cancer

The rationales for the use of neoadjuvant chemotherapy (NACT) are multiple and include reducing the tumor size, expediting the elimination of micrometastasis, improving operability and surgical down-staging (Robova et al., 2010). Since the first publication by Friedlander in 1983 on the use of primary chemotherapy in cervical carcinoma, retrospective reviews, meta-analyses, and clinical trials have examined the data on NACT (Friedlander et al., 1983). There are no large-scale patient series of outcomes when only chemotherapy is given without surgery or radiation therapy.

Neoadjuvant chemotherapy has used combinations of two to four drugs predominantly with a platinum backbone (Duenas-Gonzalez et al., 2003; Termrungruangert et al., 2005; Zanaboni et al., 2013). Table 3 lists the various drug combinations that have been studied and are currently used in Bangladesh. The standard regimens use two to three cycles of chemotherapy followed by radical hysterectomy, radiation, or both surgery and radiation. There are no trials that have



Fig. 3. Patients waiting for registration for radiotherapy, Dhaka Medical College Hospital.



Fig. 4. Day Chemotherapy Center, Dhaka Medical College Hospital.

Table 3

Drug combinations for neoadjuvant chemotherapy for cervical cancer.

Vincristine, Cisplatin, Bleomycin (VPB)
Bleomycin, Vincristine (Oncovorin), Mitomycin, Cisplatin (BOMP)
Cisplatin, Mitomycin C, 5-Fluorouracil
Cisplatin, Ifosfamide
Paclitaxel, Cisplatin, Ifosfamide (TIP)
Paclitaxel, Cisplatin weekly
Cisplatin, Topotecan
Carboplatin, paclitaxel
Cisplatin, Gemcitabine

used chemotherapy for six months while awaiting radiotherapy, which is a more common scenario in LMICs.

NACT could be a good modality to decrease the size of tumors. Cisplatin, vinblastine, and bleomycin were used before radical hysterectomy in stage I and IIA tumors larger than 4 cm; complete response rate was reported in 44% and partial response rate in 50% patients (Kim et al., 1989). Better projected 4-year disease-free survival rates were reported when neoadjuvant chemotherapy was added to radical hysterectomy plus postoperative radiotherapy in patients whose tumors were larger than 4 cm (Sardi et al., 1997). But, in a subsequent randomized trial, it was reported by the gynecologic oncology group (GOG) that no significant difference in recurrence rates (relative risk, 0.998) or death rates (relative risk, 1.008) for patients who did or did not receive neoadjuvant chemotherapy before radical hysterectomy (Eddy et al., 2007). In many other trials, comparisons between radiotherapy alone versus neoadjuvant chemotherapy followed by hysterectomy plus or minus postoperative radiotherapy were done with conflicting results. (Benedetti-Panici et al., 2002; Chang et al., 2000).

The use of triplet therapy with two cycles with bleomycin, cisplatin and vincristine followed by either radical surgery or radiation reported a 2-year follow-up in one hundred fifty-one patients (107 stage IIB and 44 stage IIIB) (Sardi et al., 1990). Recurrence and survival were related to initial clinical and pathological response to chemotherapy. For the group of good responders, 96% were alive without evidence of cancer at two years. For patients who had no tumor reduction with NACT, only 33% were alive at two years. In addition, in this retrospective study, tumor sizes < 5 cm had equivalent outcomes with surgery or radiation but larger tumor had worse pelvic control with radiotherapy.

Toxicity and antitumor activity of a multidrug neoadjuvant regimen consisting of cisplatin, ifosfamide, and paclitaxel was evaluated in bulky and locally advanced cervical cancer (Zanetta et al., 1998). Thirty-eight patients with pathologically confirmed squamous-cell cervical cancer (27 IB2-IIA, two IIB, eight IIIB, and one IVA) were prospectively enrolled in their study. Treatment consisted of paclitaxel (175 mg/m² given over 3 h on day 1), cisplatin 50 mg/m² (75 mg/m² in 10 patients), ifosfamide 5 g/m² in a 24-h continuous infusion, and

mesna. Eleven patients achieved complete clinical response, 21 had partial response, five had stable disease, and one had progression of disease. Grade 3–4 neutropenia was recorded for 71% patients, grade 3–4 thrombocytopenia for 10.5%, and grade 2 peripheral neuropathy for 2.5%. They concluded according to pathology examination, that this regimen yielded a 34% complete and optimal partial response rate with acceptable toxicity.

A 10-year follow-up reported on 80 patients with locally advanced stage IB–IIB cervical cancer with tumor diameter of more than or equal to 4 cm, after NACT by vincristine, cisplatin, bleomycin and radical hysterectomy. The study showed a reduction in tumor size after NACT in 75 cases. Overall, 5- and 10-year disease-free actual survival rates were 82% and 79.4%, respectively (Hwang et al., 2001).

A prospective randomized clinical study where 192 patients of squamous cell carcinoma of the uterine cervix in Stages Ib–Iib were randomized to one of the following treatments: Three courses of NACT with vincristine, cisplatin, bleomycin (NACT arm; $n = 106$); conventional surgery or radiotherapy alone (RT Alone arm; $n = 86$) (Napolitano et al., 2003). One hundred and fifty-six patients in Stage Ib–Iib ($n = 86$, NACT arm and $n = 70$, RT alone arm) and 16 patients in Stage III (NACT arm) who were sensitive to the NACT, underwent radical hysterectomy. The 5-year overall survival rates for the NACT and RT alone arm, respectively, were 78.6% and 73.2% in Stages Ib–IIa ($P = NS$), 68.7% and 64.3% in Stage Iib ($P = NS$). A 5-year disease-free survival rate for the NACT arm and RT alone arm, respectively, of 77.1% and 64.3% in Stages Ib–IIa ($P < 0.05$), 56.2% and 57.1% in Stage Iib ($P = NS$) was found. The study concluded that the responsiveness of cervical cancer to NACT allows surgical treatment in a larger number of patients and results in longer overall and disease free survival.

Another trial compared an ifosfamide-cisplatin doublet to a paclitaxel-ifosfamide-cisplatin (TIP) triplet in the neoadjuvant setting (Buda et al., 2005). A total of 204 patients with disease stages IB2–IVA were randomized to receive one of the regimens for three cycles before surgery. Postoperative radiotherapy was administered for lymph node infiltration, pathologically positive margins, suboptimal response, or parametrial invasion.

The primary endpoint was response rate, defined as the sum of pathological complete remissions and excellent partial remissions (residual tumor with stromal invasion < 3 mm). The response rate was significantly higher statistically with the TIP regimen (48% vs. 23% with the doublet), but TIP was associated with higher hematological toxicity. Unfortunately, no statistically significant differences in progression-free survival or overall survival were detected, although a trend in favor of the TIP regimen was observed. However, patients who achieved a complete response or an excellent partial response had a significantly longer duration of survival than those with a lesser

response.

A prospective study of patients with stage IB2 - IIB disease were randomized to undergo surgical management with or without NACT using the triplet cisplatin, mitomycin C, and 5-fluorouracil (Chen et al., 2008). Post-operative pelvic radiotherapy was used for patients with lymph node metastases, parametrial or vaginal involvement, lymph vascular space invasion, and/or ovarian metastases. Overall, almost 70% of patients had either a complete or partial response to chemotherapy. Pathologic findings were significantly reduced, with decreased pelvic lymph node metastases (25.0% vs. 42.9%, $P = 0.02$) and parametrial involvement (25.0% vs. 41.4%, $P = 0.04$). Those who responded to chemotherapy had fewer recurrences compared to non-responders (16.3% vs. 47.4%, $P = 0.01$). There was a significant difference in the 4-year overall survival between treatment arms (71.0% with NACT vs. 58.0% with control, $P = 0.04$).

A single institution series reviewed their 10 years' experience with high-dose-density NACT in cervical cancer management in 141 women. Their study revealed High-dose-density NACT and radical surgery has resulted in high clinical response rates and seemed to be feasible in the management of stage IB bulky cervical cancer. NACT-reduced tumor volume and positivity of lymph nodes and thus minimized the need for postoperative radiotherapy or chemoradiotherapy. Early and especially late toxicity of high-dose density chemotherapy was within acceptable limits. Five-year survival in patients, who underwent surgery in their study, was 80.6% (Robova et al., 2010). Despite these encouraging results in favor of NACT, there are several objections to be considered in this study. In fact, 28% of patients in group 2 did not receive intracavitary radiation; moreover, patients who underwent external radiation therapy only had a median total dose of 61.1 Gy that could be considered inadequate, and the median time of radiation treatment delivery was quite long (8.8 weeks). Furthermore, radiation therapy not in combination with chemotherapy is not anymore the standard of care for patients. Moreover, in a separate analysis by stage subgroups, patients with stage III cervical cancer did not show any significant benefit. In this group of patients, the evaluation of surgical specimens revealed a higher incidence of persistent tumor in the parametria and lymph nodes compared with stage IB2-IIB cervical cancer.

Bleomycin, vincristine, mitomycin, and cisplatin were prospectively compared to no NACT for bulky stage Ib2 to IIB cancers (Katsumata et al., 2013). NACT did not improve overall survival but reduced the number of patients needing radiation.

Because of the range of therapies and post chemotherapy treatment, many systematic reviews and meta-analyses have tried to summarize the overall benefit of NACT. A systematic review of 30 studies (between 1997 and 2012) examined the role of chemotherapy followed by surgery in 1760 patients with bulky Stage Ib2 to Stage IIIb cancers (Osman, 2014). Platinum doublets were most commonly used with a 2.7 mean number of chemotherapy cycles. Chemotherapy achieved an objective response rate of 84%. For stage IB2- IIA patients, the mean 5-year progression-free survival (PFS) was 72% and the 2-year overall survival (OS) was 83.4%. The mean 5-year PFS was 72%, and the mean 5-year OS was 83.4%. For stage IIB-IIIb, the mean 5-year PFS was 58.9%, and the mean 5-year OS was 62%.

The Neoadjuvant Chemotherapy (NACT) for Cervical Cancer Meta-analysis Collaboration performed two separate treatment comparisons that were included in their analysis: Comparison 1, in which NACT followed by local treatment was compared with the same local treatment (mainly radiotherapy) alone, and comparison 2, in which a combination of NACT followed by surgery (with or without radiotherapy) was compared with the (then) more standard radiotherapy alone (NACT, 2003).

Comparison 1 was based on 2074 patients from 18 trials; the median follow-up across all trials was 5.7 years for surviving patients. Almost 70% of patients had advanced disease (stage II or III). The study results showed that the addition of NACT to local therapy (mainly radiotherapy) did not have any impact on overall survival (hazard ratio

[HR] = 1.05; 95% confidence interval [CI]: 0.94–1.19), disease-free survival (HR = 1.00; 95% CI: 0.88–1.14), or loco-regional disease-free survival (HR = 1.03; 95% CI: 0.9–1.17). However, a highly significant level of statistical heterogeneity was evident for each of the outcomes measured; viz. P value for survival was 0.0003. It was suggested that chemotherapy may select the radioresistant cellular clones due to cross-resistance between certain chemotherapy agents and radiotherapy.

Comparison 2 of the meta-analysis compared NACT followed by surgery (with or without subsequent radiotherapy) to radical radiotherapy alone. That analysis comprised 5 randomized trials with a total of 872 patients. The planned total dose of cisplatin was between 100 mg/m² and 300 mg/m² in 10–21-day cycles; external radiotherapy and intracavitary radiotherapy doses in the radiotherapy alone arm were similar across trials (45–60 Gy and 25–40 Gy, respectively). The results of the second comparison suggested a highly significant effect of NACT, with an HR of 0.65 ($P = 0.00004$), which translates into an absolute gain in 5-year overall survival of 14% (from 50% to 64%) (NACT, 2003).

A Cochrane review examined six randomized controlled trials comparing NACT with surgery vs. surgery alone in women with early or locally advanced cervical cancer who had not undergone any prior treatment likely to interfere with the treatment comparison (Rydzewska et al., 2010). Progression Free Survival (PFS) was significantly better with NACT (HR = 0.76, 95% CI = 0.62 to 0.94, $P = 0.01$), but no Overall Survival benefit (OS) was observed (HR = 0.85, 95% CI = 0.67–1.07, $P = 0.17$). Furthermore, their analysis estimated both local (OR = 0.76, 95% CI = 0.49–1.17, $P = 0.21$) and distant recurrence (OR = 0.68, 95% CI = 0.41–1.13, $P = 0.13$) and rates of resection (OR = 1.55, 95% CI = 0.96–2.50, $P = 0.07$), either of which were in favor of NACT. There was also no difference in the effect of NACT according to total cisplatin dose, chemotherapy cycle length or by cervical cancer stage.

In Summary, the strategy of NACT has been adopted in Bangladesh to overcome the scarcity of radiation therapy and address the long waiting time. The primary objectives of NACT in the treatment of cervical cancer include improvement in tumor characteristics to allow prolonged disease-free and overall survival, and a reduction in the need for radiation therapy. The data from multiple, heterogeneous studies have consistently reported a pathologic response to NACT but long term survival differences between NACT followed by surgery and/or radiation versus conventional therapy are mixed. It may be that as in other cancers, a subset of women with advanced cervical cancer benefit from NACT. Upon review of the available evidence, there has been no consistently proven benefit in overall survival to NACT prior to surgery (versus surgery alone) or radiotherapy (versus chemo-radiotherapy alone). Most randomized studies include inadequate patient numbers to support robust conclusions. So the overall survival benefit (OS) of NACT is yet to be established. NACT clearly allows previously unresectable cancers to be surgically removed, an important strategy to at least reduce symptoms and allow pelvic control of the cancer.

There are both primary and secondary barriers to the development of a women's cancer program in Bangladesh. The challenges range from the need for subspecialty training, personal education on the prevention of hospital acquired infections, to significant infrastructure problems, and lack of access to care for patients who are impoverished or live at a distance from a healthcare facility. Increased access to radiation is crucial and until more facilities are available, there will be the continued use of primary chemotherapy to treat of women with cervical cancer. The development of a hospital specific and national tumor registry to track outcomes is crucial to understand the impact of primary chemotherapy on cervical cancer as well as to critically improve the quality of care for women with gynecologic cancers in Bangladesh.

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References

- Atun, R., Jaffray, D.A., Barton, M.B., Bray, F., Baumann, M., Vikram, B., Hanna, T.P., Knaul, F.M., Lievens, Y., Lui, T.Y., Milosevic, M., O'Sullivan, B., Rodin, D.L., Rosenblatt, E., Van Dyk, J., Yap, M.L., Zubizarreta, E., Gospodarowicz, M., 2015. Expanding global access to radiotherapy. *Lancet Oncol.* 16, 1153–1186.
- Benedetti-Panici, P., Greggi, S., Colombo, A., Amoroso, M., et al., 2002. Neoadjuvant chemotherapy and radical surgery versus exclusive radiotherapy in locally advanced squamous cell cervical cancer: results from the Italian multicenter randomized study. *J. Clin. Oncol.* 20 (1), 179–188.
- Buda, A., Fossati, R., Colombo, N., Fei, F., Floriani, I., Alletti, D.G., et al., 2005. Randomized trial of neoadjuvant chemotherapy comparing paclitaxel, ifosfamide, and cisplatin with ifosfamide and cisplatin followed by radical surgery in patients with locally advanced squamous cell cervical carcinoma: the SNAP01 (Studio Neo-Adiuvante Portio) Italian Collaborative Study. *J. Clin. Oncol.* 23, 4137–4145.
- Chang, T.C., Lai, C.H., Hong, J.H., Hsueh, S., et al., 2000. Randomized trial of neoadjuvant cisplatin, vincristine, bleomycin, and radical hysterectomy versus radiation therapy for bulky stage IB and IIA cervical cancer. *J. Clin. Oncol.* 18 (8), 1740–1747.
- Chen, H., Liang, C., Zhang, L., Huang, S., Wu, X., 2008. Clinical efficacy of modified preoperative neoadjuvant chemotherapy in the treatment of locally advanced (stage IB2 to IB) cervical cancer: randomized study. *Gynecol. Oncol.* 110, 308–315.
- Datta, N.R., Samiei, M., Bodis, S., 2014. Radiation therapy infrastructure and human resources in low- and middle-income countries: present status and projections for 2020. *Int. J. Radiat. Oncol. Biol. Phys.* 89 (3), 448–457.
- Denny, L., de Sanjose, S., Mutebi, M., Anderson, B.O., Kim, J., Jeronimo, J., Herrero, R., Yeates, K., Ginsburg, O., Sankaranarayanan, R., 2017. Health, equity, and women's cancers 2: interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. *Lancet* 389, 861–870.
- Dhaka Medical College Hospital (DMCH), 2017. Retrieved from. <https://bdeducationinfo.com/dhaka-medical-college-hospital-info/>.
- Duenas-Gonzalez, A., Lopez-Graniell, C., Gonzalez-Enciso, A., Cetina, L., Rivera, L., Mariscal, I., et al., 2003. A phase II study of multimodality treatment for locally advanced cervical cancer: neoadjuvant carboplatin and paclitaxel followed by radical hysterectomy and adjuvant chemoradiation. *Ann. Oncol.* 14 (8), 1278–1284.
- Eddy, G.L., Bundy, B.N., Creasman, W.T., Spirtos, N.M., et al., 2007. Treatment of ("bulky") stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group. *Gynecol. Oncol.* 106 (2), 362–369.
- Friedlander, M., Kaye, S.B., Sullivan, A., Atkinson, K., Elliott, P., Coppleson, M., Houghton, R., Solomon, J., Green, D., Russell, P., et al., 1983. Cervical carcinoma: a drug-responsive tumor—experience with combined cisplatin, vinblastine, and bleomycin therapy. *Gynecol. Oncol.* 16 (2), 275–281.
- Globocan, 2012. Estimated Cancer Incidence, Mortality, and Prevalence Worldwide 2012. International Agency for Research on Cancer retrieved. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.
- Grover, S., Xu, M.J., Yeager, A., Rosman, L., Groen, R.S., Chackungal, S., Rodin, D., Mangaali, M., Nurkic, S., Fernandes, A., Lin, L.L., Thomas, G., Tergas, A.I., 2015. A systematic review of radiotherapy capacity in low- and middle-income countries. *Front. Oncol.* 4, 1–11. <http://dx.doi.org/10.3389/fonc.2014.00380>.
- Hussain, S.M.A., 2013. Comprehensive update on cancer scenario of Bangladesh. *South Asian J. Cancer* 2, 279–284.
- Hussain, S.A., Sullivan, R., 2013. Cancer control in Bangladesh. *Jpn. J. Clin. Oncol.* 43 (12), 1159–1169.
- Hwang, Y.Y., Moon, H., Cho, S.H., Kim, K.T., Moon, Y.J., Kim, S.R., et al., 2001. Ten-year survival of patients with locally advanced, stage Ib-IIb cervical cancer after neoadjuvant chemotherapy and radical hysterectomy. *Gynecol. Oncol.* 82, 88–93.
- International Atomic Energy Agency (IAEA), 2011. Human Health Reports No.3, Inequality in Cancer Care: A Global Perspective. Retrieved. http://www-pub.iaea.org/MTCD/publications/PDF/Pub1471_web.pdf.
- Katsumata, N., Yoshikawa, H., Kobayashi, H., Saito, T., Kuzuya, K., Nakanisiji, T., et al., 2013. Phase III randomized controlled trial of neoadjuvant chemotherapy plus radical surgery vs radical surgery alone for stages IB2, IIA2, and IB cervical cancer: a Japan Clinical Oncology Group trial (JCOG 0102). *Br. J. Cancer* 108 (10), 1957–1963.
- Kim, D.S., Moon, H., Kim, K.T., Hwang, Y.Y., Cho, S.H., Kim, S.R., 1989. Two-year survival: preoperative adjuvant chemotherapy in the treatment of cervical cancer stages Ib and II with bulky tumor. *Gynecol. Oncol.* 33, 225–230.
- Napolitano, U., Imperato, F., Mossa, B., Framarino, M.L., Marziani, R., Marzetti, L., 2003. The role of neoadjuvant chemotherapy for squamous cell cervical cancer (Ib-IIIb): a long-term randomized trial. *Eur. J. Gynaecol. Oncol.* 24 (1), 51–59.
- (NACT) Neoadjuvant Chemotherapy for Locally Advanced Cervical Cancer Meta-analysis Collaboration, 2003. Neoadjuvant chemotherapy for locally advanced cervical cancer: a systematic review and meta-analysis of individual patient data from 21 randomised trials. *Eur. J. Cancer* 39 (17), 2470–2486.
- Osman, M., 2014. The role of neoadjuvant chemotherapy in the management of locally advanced cervix cancer: a systematic review. *Oncol. Rev.* 28 (2), 250.
- Perosky, J.E., Munro, M.L., Kay, J.L., Nyanplu, A., Williams, G., Andreatta, P.B., et al., 2015. Texting from the bush: data collection using SMS text messaging in areas of low network coverage from low-literacy providers. *J. Health Commun.* 20, 1052–1059.
- Rydzewska, L., Tierney, J., Vale, C.L., Symonds, P.R., 2010. Neoadjuvant chemotherapy plus surgery versus surgery for cervical cancer. *Cochrane Database Syst. Rev.* CD007406. <http://dx.doi.org/10.1002/14651858.CD007406.pub2>.
- Robova, H., Halaska, M., Pluta, M., Skapa, P., Strand, P., Lisy, J., Rob, L., 2010. The role of neoadjuvant chemotherapy and surgery in cervical cancer. *Int. J. Gynecol. Cancer* 20 (11), S42–S46. <http://dx.doi.org/10.1111/IGC>.
- Sardi, J.E., Giaroli, A., Sananes, C., Ferreira, M., Soderini, A., Bermudez, A., et al., 1997. Long-term follow-up of the first randomized trial using neoadjuvant chemotherapy in stage Ib squamous carcinoma of the cervix: the final results. *Gynecol. Oncol.* 67, 61–69.
- Sardi, J., Sananes, C., Giaroli, A., Maya, G., di Paola, G., 1990. Neoadjuvant chemotherapy in locally advanced carcinoma of the cervix uteri. *Gynecol. Oncol.* 38 (3), 486–493.
- Saslow, D., Solomon, D., Lawson, H.W., Killackey, M., Kulasingam, S.L., Cain, J., Garcia, F.A.R., Moriarty, A.T., Waxman, A.G., Wilbur, D.C., Wentzensen, N., Downs, L.S., Spitzer, M., Moscicki, A.-B., Franco, E.L., Stoler, M.H., Schiffman, M., Castle, P.E., 2012. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for Prevention and Early Detection of Cervical Cancer. *J. Lower Genit. Tract Dis.* 16 (3), 1–26.
- Shahida, S.M., Islam, M.A., Dey, B.R., Islam, F., Venkatesh, K., Goodman, A., 2016. Hospital acquired infections in low and middle income countries: root cause analysis and the development of infection control practices in Bangladesh. *Open J. Obstet. Gynecol.* 6 (1). <http://dx.doi.org/10.4236/ojog.2016.61004>. retrieved from. <http://www.scirp.org/journal/PaperInformation.aspx?PaperID=62917>.
- Sharma, V., Kerr, S.H., Kwar, Z., Kerr, D.J., 2011. Challenges of cancer control in developing countries; current status and future perspective. *Future Oncol.* 7 (10), 1213–1222. <http://dx.doi.org/10.2217/fon.11.101>.
- Termrungruanglert, W., Tresukosol, D., Vasuratna, A., Sittisomwong, T., Lertkhaconsuk, R., Sirisabya, N., 2005. Neoadjuvant gemcitabine and cisplatin followed by radical surgery in (bulky) squamous cell carcinoma of cervix stage Ib2. *Gynecol. Oncol.* 97 (2), 576–581.
- Uddin, A.F.M.K., Khan, Z.J., Islam, J., Mahmud, A., 2013. Cancer care scenario in Bangladesh. *South Asian J. Cancer* 2 (2), 102–104. <http://dx.doi.org/10.4103/2278-330X.110510>.
- Weinshel, K., Dramowski, A., Hajdu, Á., Jacob, S., Khanal, B., Zoltán, M., et al., 2015. Gap analysis of infection control practices in low- and middle-income countries. *Infect. Control Hosp. Epidemiol.* 22, 1–7.
- World Bank, 2017. Bangladesh Poverty and Equity. Retrieved. <http://povertydata.worldbank.org/poverty/country/BGD>.
- Worldometer, 2017. Bangladesh Population. retrieved. <http://www.worldometers.info/world-population/bangladesh-population/>.
- Zanaboni, F., Grijuela, B., Giudici, S., Cormicio, G., Babilonti, L., Ghezzi, F., et al., 2013. Weekly topotecan and cisplatin (TOPOCIS) as neoadjuvant chemotherapy for locally advanced squamous cervical carcinoma: results of a phase II multicentric study. *Eur. J. Cancer* 49 (5), 1065–1072.
- Zanetta, G., Lissoni, A., Pellegrino, A., Sessa, C., Colombo, N., Gueli-Alletti, D., et al., 1998. Neoadjuvant chemotherapy with cisplatin, ifosfamide and paclitaxel for locally advanced squamous-cell cervical cancer. *Ann. Oncol.* 9, 977–980.
- Zubizarreta, E.H., Fidarova, E., Healy, B., Rosenblatt, E., 2015. Need for radiotherapy in low and middle income countries e the silent crisis continues. *Clin. Oncol.* 27, 107–114.