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Efforts towards erasing borders in gynecologic cancer?

Advances in medicine and heroic efforts by the global community have saved millions from death from HIV and other infectious diseases over the past twenty years. Yet that effort, which has been of truly historic proportions, is not enough: the incidence of global cancer is predicted to rise dramatically from 17 million in 2012 to 23.6 million by 2030, and more than 50% of all cancers occur in low and middle-income countries (LMICs) (IARC, 2012). In addition, 65% of all deaths caused by cancer occur in LMICs. Cervical cancer is the most common gynecologic cancer and second most common cancer among women in LMICs. In half of the Sub-Saharan countries, it is the most common women cancer (Denny and Anorlu, 2012). The prevention, screening, and treatment of cervical cancer in these countries are often impacted by social and economic disparities. Increased efforts dedicated to improving cervical cancer care, education, and research in LMIC are urgently needed.

Human Papillomavirus (HPV) is the primary causative pathogen for the majority of cervical cancers (Bosch et al., 2013). HPV vaccines, Gardasil and Cervarix, have been available for the last decade. These vaccines offer protection against oncogenic pathogens HPV 16 and 18 and are approved in 100 countries. The new nonavalent (Gardasil 9) vaccine offers coverage against 5 additional HPV types (31, 33, 45, 52 and 58) which can potentially protect women from 90% of cervical cancer causing HPV. Low cost vaccines are currently available through GAVI Alliance to half of the world's poorest nations for less than $5 per dose. Robust HPV vaccination programs have thus far been available in limited countries in the world. It will take decades for its implementation and much longer before substantial reduction of cervical cancer materializes. In our special issue, Nakisige and her colleagues addressed the challenges and the importance of a robust HPV vaccination in, Uganda (Nakisige et al., 2017).

In 2012, 85% of cervical cancer incidences and 87% of related deaths occur in LMIC. The major contributing factor for greater occurrences in LMIC is a lack of screening program implementation. A multitude of obstacles including poverty, limited public information and knowledge, social and cultural barriers, the absence of sustainable and effective screening programs, and competing public health programs exist. In high-income countries (HIC) where screening programs are available, the incidence of cervical cancer has decreased by nearly 80% in the last 40 years since the induction of the programs (Sankaranarayanan et al., 2001), thus demonstrating their effectiveness. Cervical cancer screening with traditional cytology and HPV co-testing is not feasible in LMIC due to the lack of pathology laboratories, cytologists, and referral infrastructure (Catarino et al., 2015). While 63–90% of women in HIC had cervical cancer screening, the screening rate in LMIC such as Bangladesh was reported to be as low as 1% (Gakidou et al., 2008). In a recently published ASCO resource stratified guideline, HPV DNA testing is recommended in all countries other than in settings where resources are limited, visual assessment using acetic acid or Lugol's solution is the next best alternative screening strategy (Jeronimo et al., 2016). The age and interval of screening vary depending on available resources and infrastructures. For HIC, screening is recommended with cytology and HPV contesting or primary HPV screening every 5 years beginning at the 25 years and terminates at 65 years in low-risk women. Fewer screening frequencies are recommended dependent on available resources. In LMIC with very basic infrastructure, one to three times per lifetime between 30 and 49 years may offer the best strategy in cervical cancer disease control. In the manuscript by Nakisige in this special issue, efforts in organizing VIA and HPV DNA testing on self-collected samples were reported. Based on their finding, a national, large-scale population-based screening program was thought to be feasible in Uganda. Cremer et al. reported the implementation of a nationwide screening program in El Salvador using careHPV tests (Cremer et al., 2017). Additional research in implementation and improvement in healthcare infrastructure is needed for other LMIC.

Because of the lack of cervical cancer screening in LMIC, most women with new cervical cancer are diagnosed at an advanced stage and require chemoradiation therapy. A strict adherence of these treatment protocols may not be applicable in certain LMIC countries. Pereira and Henriquez Cooper et al. reported women with locally advanced cervical cancers in Honduras who were treated with sporadic non-platinum chemoradiation had an inferior outcome comparing to women who were treated with radiation alone (Pereira et al., 2017). The treatment inferiority was a result of prolonged treatments and the authors emphasized the importance of completion of treatment within 55 days rather than delaying the treatment because of the unpredictable availability of cisplatin chemotherapy. The lack of radiation machines is a common occurrence in LMIC and in nearly half of the African countries, there are no radiation machines to treat women with advanced cervical cancers (GTFRCC, 2014; Abdel-Wahab et al., 2017). Alternative treatment strategies have been adopted to treat women with cervical cancer when there is no or a lack of radiation machines. These strategies include the use of neoadjuvant chemotherapy followed by possible radical hysterectomy; performing radical hysterectomy for larger cervical cancer followed by adjuvant therapy when indicated; and chemoradiation followed by extrafascial or radical hysterectomy in selected patients where brachytherapy is not available. Although there is a lack of evidence of the use of neoadjuvant chemotherapy in treating women with advanced cervical cancer, both American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) cervical cancer resource stratified treatment guidelines recommend the consideration of neoadjuvant chemotherapy in LMIC where there are limited or no radiation machines (Koh et al., 2015; Chuang et al., 2016a). Results from the two international prospective randomized trials (EORTC 55994 and

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NCT00193739) comparing neoadjuvant chemotherapy followed by surgery to standard chemoradiation may add new evidence for this treatment strategy.

In the past decade, there are increasing global efforts in the education and training for residents and oncologic surgeons. Novel platforms including online education curriculum and video surgical teachings have been developed to overcome challenges imposed in LMIC which include budget constraints and unstable infrastructures (Autry et al., 2013). Onsite teaching programs have been developed in LMIC to teach residents on gynecologic oncology (Schmeler et al., 2013; Chuang et al., 2014). Formal two-year gynecologic oncology fellowship training have recently been developed in Kenya, Ghana and, Ethiopia (Johnston et al., 2017). The International Gynecologic Cancer Society is developing a larger scale international gynecologic oncology global curriculum and training program for other LMIC (Chuang et al., 2016b). The curriculum and the scope of training will vary in different regions of the world. Adaption to local cultures is paramount (Johnston et al., 2017). Equally if not more important in improving cancer care is the development of clinical trials targeted specifically to LMIC. Successes and challenges of conducting clinical trials in LMIC were reported by Grover et al. in this special issue (Grover et al., 2017). Lastly, it is often observed that clinical presentations and outcomes often appear to be different in LMIC. Whether this is due to social and economic circumstances, biology, or both is unclear; this begs the question of whether diseases require the same treatment in LMIC and they do in HIC. Randall and colleagues (in press) emphasize the importance of research in defining the burden and nature of malignancies in LMIC.

The incidence and mortality of gynecologic cancers will continue to rise in the next decade, with the majority of these new cases occurring in LMIC. Without major efforts to improve screening, treatment, education and research, this trend is expected to continue its current trajectory. Gynecologic Oncology Reports hopes to provide a platform featuring commentary, research and reviews of the current status and provide future directions by global leaders and experts in gynecologic cancers to and from LMIC.

Conflict of interest

The authors report no conflicts of interest.

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