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Investigating the Nexus between Gynaecologic Cancer and Human Development Index

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Abstract

This study aimed to describe the current incidence and mortality rates of gynecologic cancer and their association with socio-economic development. The data for the age-standardized incidence rate (ASRI) and age-standardized mortality rate (ASRM) were acquired from the GLOBOCAN-2012 database. Human Development Index (HDI) data were obtained from the 2015-Human Development Report. The correlation between HDI and Mortality to Incidence Ratio (MIR) was assessed by Pearson-correlation. The effect of national-HDI on MIR was analyzed by linear regression analysis. The ASRI, ASRM, and MIR of cervix cancer were higher in the less developed regions (LDRs) than in more developed regions (MDRs). However, for corpus uteri cancer, the ASRI was 3.6 times and the ASRM was 1.5-times higher in the MDRs than in the LDRs. Strong inverse associations between MIR and HDI were reported from cervix (adjusted $R^2 = 0.825$, $\beta = -0.908$, $p < 0.001$), corpus uteri (adjusted $R^2 = 0.554$, $\beta = -0.746$, $p < 0.001$) and ovarian cancer (adjusted $R^2 = 0.579$, $\beta = -0.763$, $p < 0.001$). The higher MIR of gynecologic cancer in LDRs demand for sustainable investment in health systems and balanced cancer control plans in the region. *(Afr J Reprod Health 2020; 24[1]: 53-61).*

Keywords: Gynecologic cancer, epidemiology, socioeconomic status

Résumé

Cette étude visait à décrire les taux actuels d'incidence et de mortalité du cancer gynécologique et leur association avec le développement socio-économique. Les données relatives au taux d'incidence normalisé selon l'âge (INSA) et au taux de mortalité normalisé selon l'âge (TMNSA) ont été obtenues à partir de la base de données GLOBOCAN-2012. Les données de l'indice de développement humain (IDH) ont été obtenues à partir du rapport de 2015 sur le développement humain. La corrélation entre l'IDH et le rapport mortalité / incidence (RMI) a été évaluée par corrélation de Pearson. L'effet de l'IDH national sur le RMI a été analysé par analyse de régression linéaire. L'INSA, le TMNSA et le RMI du cancer du col de l'utérus étaient plus élevés dans les régions moins développées (RMD) que dans les régions plus développées (RPD). Cependant, pour le cancer du corps utérin, l'INSA était de 3,6 fois et Le TMNSA était 1,5 fois plus élevé dans les RPD que dans les RMD. De fortes associations inverses entre le RMI et l'IDH ont été signalées dans le col de l'utérus (R2 ajusté = 0,825, β = - 0,908, p <0,001), le corps utérin (R2 ajusté = 0,554, β = - 0,746, p <0,001) et le cancer de l'ovaire (R2 ajusté = 0,579, β = - 0,763, p <0,001). Le RMI plus élevé du cancer gynécologique dans les RMD exige un investissement durable dans les systèmes de santé et des plans de lutte contre le cancer équilibrés dans la région. *(Afr J Reprod Health 2020; 24[1]: 53-61).*

Mots-clés: Cancer gynécologique, épidémiologie, état socio-économique

Introduction

The cancer burden is increasing worldwide[1]. The incidence and mortality of different cancer types vary in different countries and even between sexes in the same country[2,3]. The cancer types that were most frequently diagnosed in developed countries, such as lung cancer in men (1.8 million) and breast cancer in women (1.7 million), are now being diagnosed with a greater incidence rate in developing countries[4].

Due to improvements in early detection, the death rate for some cancer types has decreased, despite an increase in their incidence rate[2].

Additionally, in the countries with an increasingly aging population, such as the United States, the introduction of new diagnostic tools for the early detection of cancer and new specific targeted therapies has increased the cost of cancer care[5].

A wide range of variations exists in the incidence of malignant tumors of the female gynecologic system. The global age-standardized rate of incidence (ASRI) per 100,000 for gynecologic cancer types in women ranges from the rare vaginal cancer (ASRI 0.8) and vulvar cancer (ASRI 1.5 in developed countries and less than 1.0 in developing countries) to the more frequently occurring cervical cancer (ASRI 14.0), which is also the main cause of cancer mortality in developing countries[6].

Differences in the exposure to various risks, such as lifestyle, reproductive, hormonal and dietary factors, as well as the availability of medical facilities and health systems for different types of cancer reflect the international variations in the cancer burden[7]. The relationship between the global incidence and mortality of gynecologic cancer and socio-economic development is not clear at present.

Therefore, this study aims to compare the incidence and mortality of cervix uteri, corpus uteri, and ovarian cancer at a national and regional level, and to determine the correlation between these three types of gynecologic cancer burden and the socioeconomic development of countries.

Methods

Data collection

Based on the availability of recent and complete data, the data for the age-standardized rate of incidence (ASRI) and age-standardized rate of mortality (ASRM) for cervix uteri cancer, corpus uteri cancer, and ovarian cancer was acquired from the GLOBOCAN 2012 database. The detailed method used for the collection of country-wise data and the calculation of age-standardized incidence and mortality rate of cancer with world standard population for different countries of the world are given in the GLOBOCAN database[8].

The mortality to incidence ratio (MIR) is obtained by dividing the ASRM of a country by the ASRI of the same country. The MIR provides a standard population-based estimation of survival by stabilizing the incidence and mortality differences of a cancer type in different countries. The MIR value gives an insight into the proficiency of the health system and the efficiency of cancer control programs[9].

Human development index (HDI) data of 174 countries around the world for the year 2015 were acquired from the database of the United Nations Development program[10]. HDI is the combination of three parameters: gross national per capita income, life expectancy at birth, and years of schooling, with the value ranging from 0 to 1. All countries are divided into four categories on the basis of HDI, which are low (HDI < 0.555), medium (HDI 0.550–0.699), high (HDI 0.700–0.799), and very high (HDI ≥0.800) HDI countries. A higher HDI index for a country represents a greater degree of development. For statistical convenience, the designation "more developed regions (MDRs)" and "less developed regions (LDRs)" are used. The United Nation population division has categorized all regions in Europe in addition to Northern America, Australia/New Zealand and Japan as MDRs, while all regions in Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia as LDRs[11].

Analysis

The correlation between HDI and MIR was calculated by Pearson correlation. For the assessment of the effect of HDI on the MIR, linear regression analysis was used. The assumptions of the classical linear regression model (CLRM) was identified using ARCH test for heteroscedasticity[12], Breusch Pagan Godfray serial correlation test [13], and normality test (Jarue-Bera test)[14]. All the models confirm the absence of heteroscedasticity problems in their residuals. Moreover, in all the three models the R square and adjusted R square were above 50% that is favorable in explaining the significant change of MIR of cervix uteri, corpus uteri, and ovarian cancer with HDI. The *F*-statistics of estimation showed the overall good fit of the models. The autocorrelation in all three models are showing the absence of autocorrelation problem in addition to the serial correlation test.

The significance of variance in the MIR of three types of cancer (cervix uteri, corpus uteri, and ovarian cancer) among different HDI countries was assessed by One-way ANOVA[12, 15]. Statistical analysis was performed in the SPSS version 20 and the level of significance is considered as $p \leq 0.05$.

Results

Incidence and mortality of gynaecologic cancers

The worldwide ASRI for cervix uteri cancer was 14 per 100,000. The highest incidence rates were reported in Eastern Africa (ASRI 42.7), Southern Africa (ASRI 31.5), Western Africa (ASRI 29.3) and the lowest incidence rates were reported in Western Asia (ASRI 4.4), Australia and New Zealand (ASRI 5.5), Northern America (ASRI 6.6) and Northern Africa (ASRI 6.6) (Figure 1A). The incidence rate of cervix uteri cancer was 1.6 times higher in the LDRs around the world than in the MDRs.

The world cervix uteri cancer mortality was ASRM 6.8. The highest mortality rates were reported in Eastern Africa (ASRM 27.6), Western Africa (ASRM 18.5) and Southern Africa (ASRM 17.9), while the lowest mortality rates were reported from Australia/New Zealand (ASRM 1.5), Western Europe (ASRM 1.8), and Western Asia (1.9) (Figure 1A). There was a 2.5-fold increased mortality rate of cervix uteri cancer in the LDRs of the world than that of the MDRs.

The standardized cancer incidence for corpus uteri cancer was ASRI 8.2 cases per 100,000 individuals. The highest incidence rate was reported in Northern America (ASRI 19.1), Central and Eastern Europe (ASRI 15.6) and Northern Europe (ASRI 14.1), while the lowest incidence rate was reported in South-Central Asia (ASRI 2.7), Northern Africa (ASRI 3.1) and Western Africa (ASRI 3.3) (Figure 1B). There was a 3.6-fold increase in the ASRI of corpus uteri cancer in the MDRs (5.4) compared to LDRs (1.5).

The highest corpus uteri cancer mortality was reported in Central and Eastern Europe (ASRM 3.4), Northern Europe (ASRM 2.3), Southern Europe (ASRM 2.1) and Northern America (ASRM 2.2), while the lowest ASRM were reported in Northern Africa (ASRM 0.9), South-Central Asia (1.0), Eastern Africa (1.3) and Western Africa (1.4) (Figure 1B). There was a 1.5-fold increase in the corpus uteri cancer mortality rate in MDRs than that of LDRs of the world.

For ovarian cancer, the standardized incidence rate was ASRI 6.1 cases per 100,000 individuals. The highest incidence rate was reported in Europe (ASRI 11.4-9.1), while the lowest incidence rate was reported in Western Africa (ASRI 3.6), Eastern Asia (ASRI 4.7) and South-Central Asia (ASRI 4.9) (Figure1C). There was a 1.9-fold difference in ASRI between the MDRs (9.1) and LDRs (5.0) of the world.

The highest ovarian cancer mortality rate was also reported from Europe (ASRM 6-5.9), and Northern America (ASRM 5.0), while the lowest ASRM were reported from Northern (1.9) and Western Africa (3.0), and central and South America (3.4-3.7). (Figure1C). There was a 1.6-fold difference between the ovarian cancer mortality rate of MDRs (5.0) and LDRs (3.1) of the world.

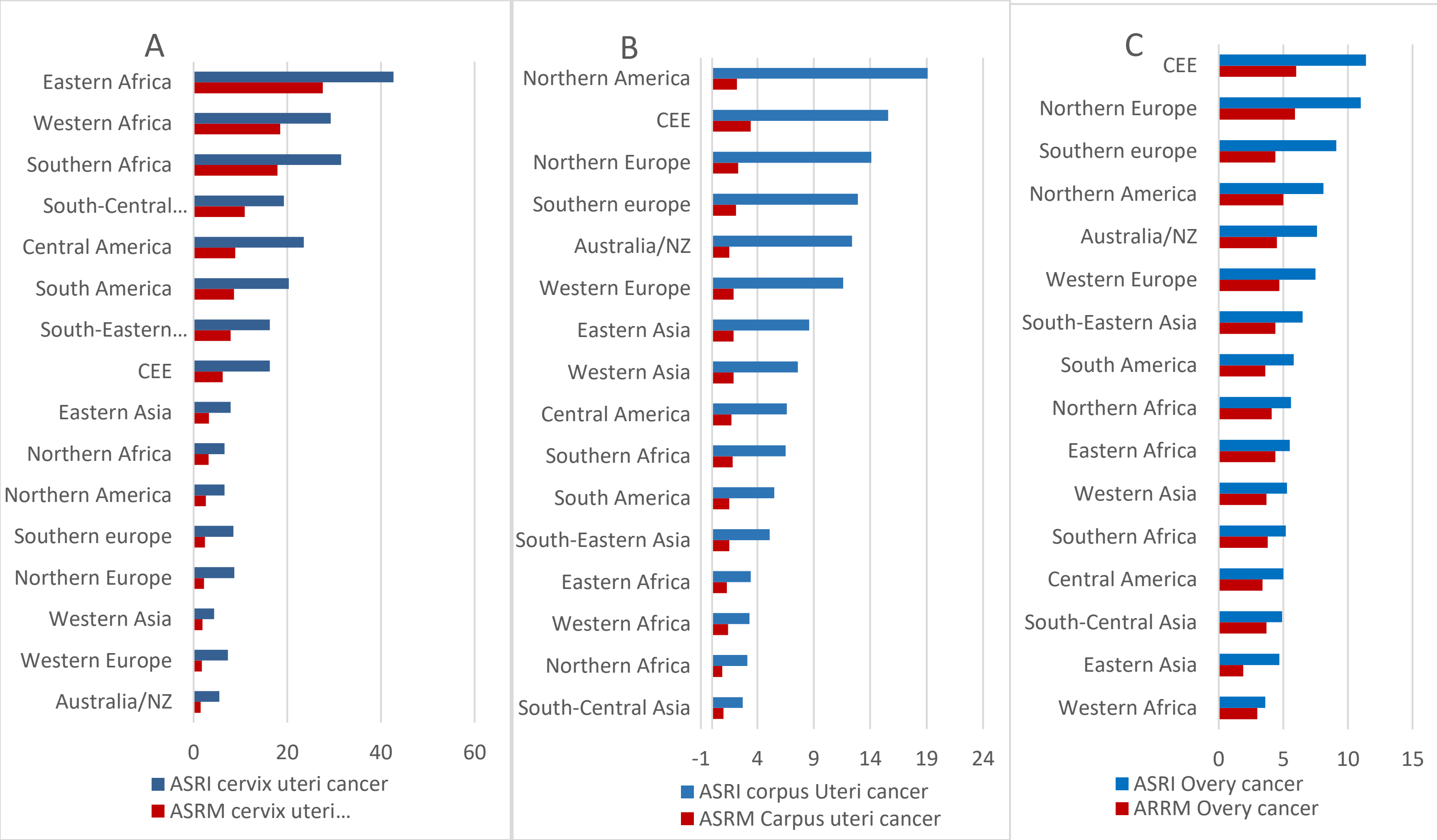
MIR of the three types of gynecologic cancers and their relation with HDI

The MIR for cervix uteri cancer (MIR = 0.68), corpus uteri cancer (MIR = 0.44) and ovarian cancer (MIR = 0.84) were significantly highest ($P < 0.001$ each) in the countries with low HDI and were lowest in the very high HDI countries (MIR = 0.32, MIR = 0.19, MIR = 0.59 respectively) (Figure 2, Table 1).

The Pearson correlation coefficient indicated that MIR has significant inverse relation with HDI (cervix cancer $r = -0.908$; $p < 0.001$, corpus cancer $r = -0.746$; $p < 0.001$, ovarian cancer $r = -0.763$; $p < 0.001$). Linear regression analysis also confirmed a strong inverse relation between HDI and MIR for cervix uteri (adjusted $R^2 = 0.825$, $\beta = -0.908$, $p < 0.001$) (Figure 3A), corpus uteri (adjusted $R^2 = 0.554$, $\beta = -0.746$, $p < 0.001$) (Figure 3B), and ovarian cancer (adjusted $R^2 = 0.579$, $\beta = -0.763$, $p < 0.001$) (Figure 3C).

Discussion

This retrospective study was based on GLOBOCAN-based data analysis for 74 countries around the world categorized into four HDI groups.



Note: CEE “Central Eastern Europe”, NZ “New Zealand”

Figure 1: Worldwide incidence and mortality of cervix uteri (A), corpus uteri (B), and ovarian cancer (C)

Figure 2: Difference in Mortality to Incidence Ratio **(**MIR) of cervix uteri ($p < 0.001$), corpus uteri ($p < 0.001$), and ovarian ($p < 0.001$) cancers in different Human Development Index (HDI) group countries

Table 1: Mean Mortality to Incidence Ratio (MIR) with standard deviations (SD) for cervix uteri, corpus uteri and ovarian cancer in countries from different HDI groups

HDI group	**No. of Countries**	**Mean ± SD ** MIR Cervix uteri cancer**	**Mean ± SD** MIR Corpus uteri cancer**	**Mean ± SD** MIR Ovary cancer**
Low HDI	41	0.68 ± 0.08	0.44 ± 0.11	0.84 ± 0.06
Medium HDI	39	0.51 ± 0.07	0.32 ± 0.09	0.77 ± 0.07
High HDI	46	0.40 ± 0.07	0.25 ± 0.10	0.63 ± 0.10
Very High	48	0.32 ± 0.10	0.19 ± 0.07	0.59 ± 0.10
Total	174	0.47 ± 0.16	0.29 ± 0.13	0.70 ± 0.13

** *P <0.001* (ANOVA probability value)

Cancer incidence and mortality rates for three types of gynecologic cancer were analyzed. As the MIR of a country is related to its health system and the efficiency of the cancer control programs[8], an inverse relationship of the cancer MIR was found with the HDI for each type of gynecological cancer. Therefore, the more developed countries had better MIR results compared to the less developed countries. The ANOVA analysis also confirmed this significant difference of MIRs of the three types of gynecologic cancers (Cervical $p < 0.001$, Corpus uterine $p < 0.001$, and Ovarian $p < 0.001$) in higher and lower HDI group countries.

Due to the disproportionate investment in cancer care and prevention[16], the cancer burden is increasing in LDRs[17]. In 2015, the World Health Organization (WHO) conducted Non-communicable diseases (NCD) Country Capacity Survey (CCS). According to their results, only 37% of African countries offered pathology

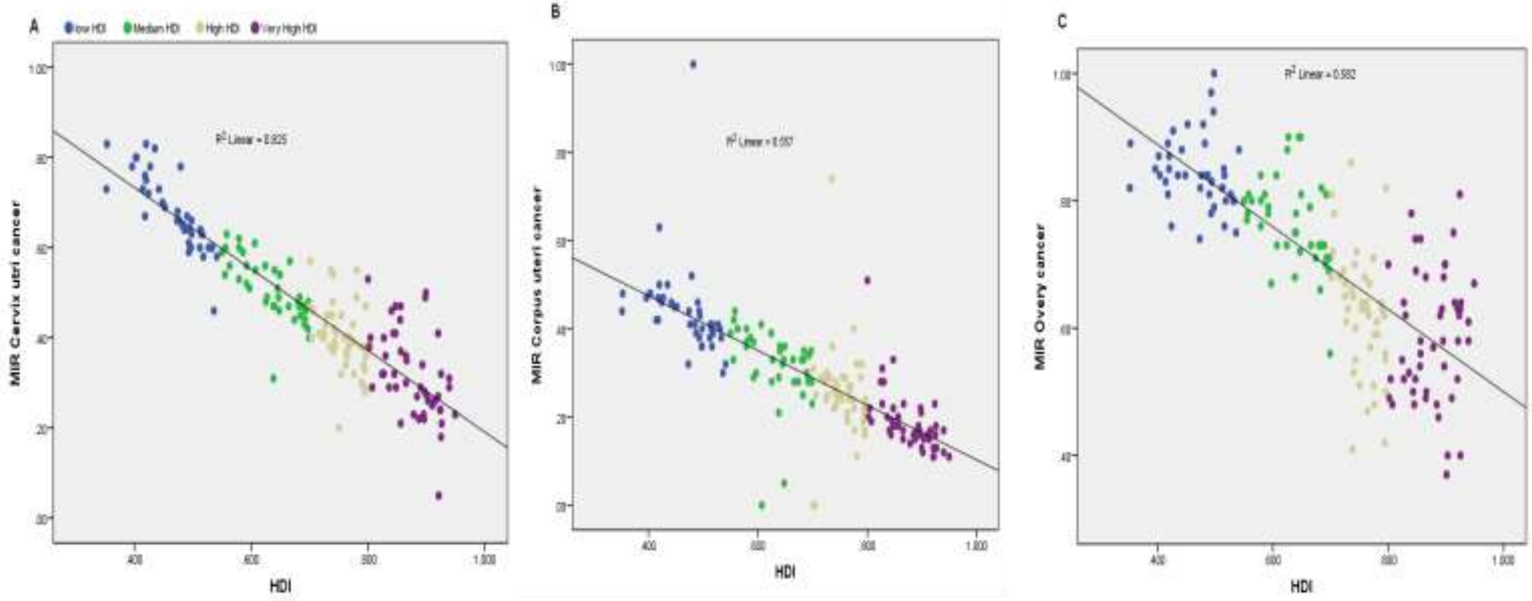


Figure 3: The effects of Mortality to Incidence Ratio (MIR) on Human Development Index (HDI) for Cervix uteri (A), Corpus uteri (B) and Ovarian cancer (C**)**

services in the public sector. Similarly, treatment services were only available in less than 30% of low-income countries and it was reported that 25% countries had no public radiotherapy centers[18].

In the LDRs, cervical cancer is the second most common cancer in women, while in the MDRs, it is ranked only 11th[19]. Globally, it is the third most commonly diagnosed cancer and the fourth most common cause of cancer mortality in women. More than 85% of cervical cancer incidence and mortality occurs in the developing countries[19]. Such a large burden of cervix uteri cancer in the developing countries is related to the impractical health systems in these countries in relation to early diagnosis and treatment[20]. There is a scarcity of facilities for Papanicolaou testing and or other types of screening tests for cervix uteri cancer. The most cost-effective testing procedures in these developing countries is DNA testing for the human papillomavirus (HPV) infection in a sample of cervical cells[21]. Also, the HPV vaccinations are only available to less than 2% of women worldwide and are generally not accessible to those countries where the cervical cancer incidence rate is very high[22].

There is a 7.1-fold difference between the incidence of corpus uteri cancer worldwide, with the highest overall incidence found in America, Europe, Australia and New Zealand. Although the mortality pattern shows a small difference, the MIR varies significantly between the different HDI group countries, where it is lower in very high-HDI countries and higher in the low HDI countries. This suggests that in the underdeveloped countries, the corpus uteri cancer patient survival rate is lower than that in the developed countries.

As corpus uteri cancer is a postmenopausal disease, with a mean age at diagnosis of 66 years, survival is strongly influenced by tumor histology, stage, grade, the patient's age at the time of diagnosis and most importantly, by the ability of the healthcare systems to diagnose and treat the cancer in its early stages[23]. The risk factors associated with corpus uteri cancer (approximately 90% of which are endometrial cancers) include obesity, abdominal fatness, hormonal replacement therapy, early menarche and late menopause, polycystic ovary syndrome, nulliparity and the use of tamoxifen[24]. This higher MIR of uterine corpus in the underdeveloped countries reflects the presence of fragile health systems in these countries in terms of the diagnosis and treatment of the disease. The five-year survival rate of corpus uteri cancer reported in Libya is only 17%[25], while in economically developed countries where the early diagnosis and treatment of corpus uteri cancer is common, the five-year survival rate is more than 75%[26].

In the case of ovarian cancer, the incidence was higher in Europe, America and New Zealand, while it was lowest in Africa and Asia, with a 3.2-fold difference. However, the MIR was lowest in the developed countries and highest in the low economic status countries. The etiology of ovarian cancer is not fully understood; however, studies have suggested that various reproductive, hormonal, biological, dietary, and genetic factors are associated with this type of cancer. Also, environmental factors, lifestyle factors, and the increasing pace of life are also associated with the increased incidence of ovarian cancer[27]. Nevertheless, the role of infection (viral and bacterial) in the development of ovarian cancer is unclear[28].

A decrease in mortality from the disease is associated with early detection, while in developing countries, ovarian cancers are mostly being diagnosed in advanced stages with poor prognosis[6]. The high mortality in relation to the incidence in developing countries reflects the significantly less favorable prognosis of ovarian cancer in comparison to that of the developed countries.

Although the highest burden of women cancers is in LDRs, only 5% of global spending on cancer is directed toward these countries[29]. Moreover, in the regions with weak health systems and scare resources, cancer contributes to the cycle of poverty. In addition to factors such as rapidly growing populations, environmental contamination, and uncontrolled infection, the developing countries are also faced with a number of unique challenges including fatalism, inequities, introspection, migration of skilled health workers, and a distrust of Western medicine[30]. Additionally, the key challenges for the capacity building and technical qualification in overall health systems are the introduction of more health institutions and health professionals, the equal supply of resources, staff and funding and the balanced delivery of cancer care[31]. Furthermore, the progress in the fight against cancer is indicated by the availability of high-quality data on cancer incidence and survival; however, in Asia, Africa and Latin America, less than 10% of the registries are reporting high-quality data[32].

Therefore, the sustainable investments in the health system, cancer care and control, vaccination for HPV, as well as the development of cancer registries in the LDRs, are the urgent needs.

It is important to note that this study had several limitations. In this study MIR is used as indicator of health system efficiency and disparities in cancer care in different countries and regions. However, its reliability depends on the accuracy of incidence and mortality data. This analysis is based on the data from GLOBOCAN for 174 countries together with the methods based on the availability of cancer incidence and mortality data at the country or regional level. Different methods of data estimation are used by GLOBOCAN, which depends upon the availability of cancer incidence and mortality data in different countries and regions. In addition to real and valid counts of cases and deaths, samples-based estimations, neighboring rates estimations and estimates have been used as the weighted average of regional rates. In such cases, there may be the possibility of overestimation of the incidence of cases if the estimate is from a single urban cancer registry in a country with a large rural population. Also, underreporting of cancer deaths in case of failure of diagnosis may also be possible. However, despite the variations in data quality and the methods of estimation, the GLOBOCAN 2012 data is the best available source and may be used in the planning and setting of priorities for cancer control programs in different countries and regions around the world. Another limitation is that this study has used the health data for 2012 based on the availability while the socioeconomic data for 2015. This time gape will result in variations in the relationship. Further studies on the most recent data with no time difference should be conducted for confirmation of these results.

Although the rate of incidence and mortality of the two gynecologic cancer types (corpus uteri and ovarian cancer) were highest in the MDRs, their MIR was highest in the countries with low socioeconomic development. In contrast, the analysis suggested that both the incidence as well as the mortality of cervix uteri cancer were highest in the LDRs. Controlling the incidence and underlying causative factors of gynecologic cancer is now a challenging target for these countries, and having a broad, well-implemented cancer control plan is a crucial part of that process.

Contribution of Authors

RP participated in the conception of the study, data acquisition, interpretation and drafting the manuscript. FF participated in the statistical analysis and revising the article for important intellectual content. Both authors read and approved the manuscript.

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