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Worldwide association of the gender inequality with the incidence and mortality of cervical, ovarian, endometrial, and breast cancers

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ABSTRACT

Background: There is a huge disparity in cancer incidence and mortality around the globe. A considerable share of this disparity can be explained by human development. Particularly in many less developed countries, women have been hindered in their human development. In this ecological study, we hypothesize that, notwithstanding acceptable overall development in countries, gender inequalities might affect the incidence and mortality of women's malignancies, and there is a distinct association between them.

Method: The data on the incidence and mortality of gynecologic and female breast cancers were retrieved from the GLOBOCAN database, and the data on the Human Development Index (HDI), Gender Development Index (GDI), and Gender Inequality Index (GII) were obtained from the United Nations Human Development Report. The Poisson regression modeling was then used to fit four models for each cancer.

Result: GII and GDI are both significantly associated with incidences of women's cancers, except for the insignificant association between GDI and the incidence of ovarian cancer. However, the association between GDI and the mortality of women's cancer is not strong. At the same time, there are significant direct relationships between GII and the mortality of breast, cervical, and endometrial cancer.

Conclusion: The incidence and mortality of women's cancers are ecologically associated with the country-level gender inequality captured with GDI and GII.

1. Introduction

Gender inequality in health is a major and common problem worldwide, resulting from societal norms and deep-seated biases that view women as more expendable than men (Global gender equality in 2023, 2023; Okojie, 1994). Gender inequality remains prevalent, particularly in less developed countries where unequal health access, unequal political representation, economic gaps, and inadequate legal defenses contribute to lower women's Human Development Index (HDI) than men's. The gender-based difference in HDI is associated with factors such as lower income and educational attainment for women, resulting in lower social status (Veas et al., 2021). This leads to worse health outcomes for women (Health CoSDo, 2008) (but also men (Shannon et al., 2019)) due to limited access to healthcare services following lower income and education levels. The level of importance of this issue is so high and universal that International organizations, such as UNDP (Sustainable development goals, 2015) and WHO's "Health for All" campaign (World Health O, 2019), have set goals (the fifth goal of Sustainable Development) to address this issue and achieve gender equality.

WHO's "Health for All" campaign emphasizes the importance of accessible healthcare, addressing social determinants of health such as gender inequality, empowering individuals and communities, promoting health equity, and reducing disparities (World Health O, 2019). "Health for All" is hindered by the uneven distribution of resources and access, creating a cycle of poverty and poor health, leading to worsening

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disparities between nations, genders (Fig. 1), races, and social minorities, to name a few (Organization, 2003; Veas et al., 2021). Accordingly, women in societies with higher levels of gender inequality experience poorer health outcomes, such as higher mortality and morbidity, than women in more egalitarian societies (Marmot, 2005; Sen & Östlin, 2008).

Among the major causes of women's morbidity and mortality across the globe are Breast and Gynecologic cancers (Okojie, 1994). According to the GLOBOCAN 2020, global age-standardized incidence and mortality rates (per 100,000 women) of these cancers were 47.8 and 13.6 for female breast cancer (BC), 13.3 and 7.3 for cervical cancer (CC), 8.7 and 1.8 for endometrial cancer (EC); and 6.6 and 4.2 for ovarian cancer (OC) (Cancer IAfRo, 2020). As measured by HDI - a tool to quantify the level of human development based on health, education, and standard of living (UNDP, 2019)- Healthcare accessibility, social development, and contextual disparities are attributed, in part, to the varying incidence and mortality of these malignancies among populations, hindering the goal of achieving Health for All (Bray et al., 2012; Fidler et al., 2016; Kogevinas et al., 1997). Additionally, recent studies have shown that HDI is correlated with the incidence (direct association) and mortality (inverse association) of EC, BC, and OC (Fidler et al., 2016; Hu et al., 2016; Martínez-Mesa et al., 2017). In contrast, an inverse correlation between mortality and incidence of CC and HDI has been reported (Fidler et al., 2016; Singh et al., 2012).

HDI, as an aggregated index, is estimated for a population. Therefore, while using it, the fact that there may be differences between subpopulations of a country regarding the level of human development is ignored. Such disparities and marginalization are expected across socioeconomic groups, genders, and ethnicities (Marmot, 2005; Veas et al., 2021). Moreover, the social determinants of health framework propose that social factors such as gender, race, and socioeconomic status play a significant role in health outcomes (Benigni, 2007; Marmot, 2005). Furthermore, Intersectionality theory in health recognizes that health is shaped by multi-dimensional overlapping factors such as race, poverty status, education, age, ability, gender, sexual orientation, religion, indigeneity, and geography (Women UNEfGEatEoWU and Kabir, 2021). It is a framework to investigate the deep roots of social inequalities and describe how systems of power and oppression interlock to shape people's lived experiences, health, and well-being, based on their multiple identities (Vohra-Gupta et al., 2023; Women UNEfGEatEoWU and Kabir, 2021). Therefore, gender inequality, one of the nuisances of such disparities, can lead to substantial health inequalities

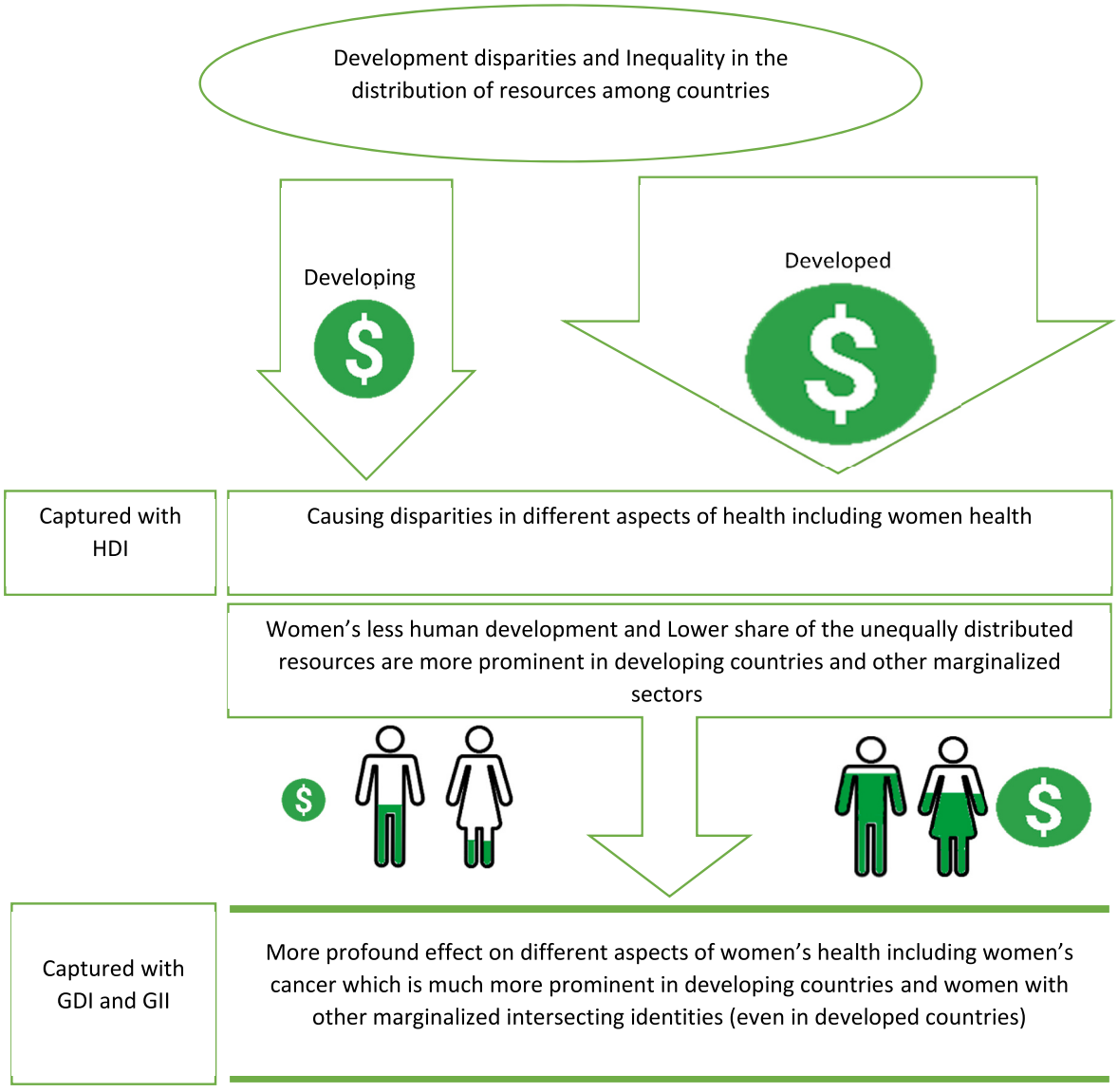

Fig. 1. Graphical abstract of theoretical framework depicting the different levels of development and resource distribution which results in disparities between countries and the most prominent effect of this disparity on women in developing countries and other marginalized sectors.

(Okojie, 1994; Veas et al., 2021; Vohra-Gupta et al., 2023). Because the average HDI value for women is 5.9 percent lower than that of males globally (0.705 vs 0.749), just using HDI as a component indicating general societal development may be inaccurate in analyzing the influence of social development on women's health-related events (UNDP, 2019).

Among composite indices introduced to capture gender inequality are gender development and gender inequality indices. The Gender Development Index (GDI) is an important means for evaluating gender disparity since it assesses women's and men's empowerment in three critical domains: health, education, and income (UNDP, 2019). The Gender Inequality Index (GII) is another indicator that measures gender inequality in three dimensions: reproductive health, empowerment, and labor market (UNDP, 2019).

Many studies have mentioned specific gender-based health disparities in the incidence and mortality of different cancers (Benigni, 2007; Lautner et al., 2015; van der Ham et al., 2021; Veas et al., 2021). These inequalities may be due to a range of factors, including differences in access to cancer screening and treatment, as well as gender-based differences in cancer risk factors such as smoking and alcohol consumption (Sabatino et al., 2012; Samet et al., 2010; Vohra-Gupta et al., 2023). Therefore, to better understand the linkage between Gender Inequality and health inequality, we will incorporate a theoretical framework that illustrates how gender inequality influences women's health outcomes in an exclusive aspect of women's health, cancers specifically affecting women (Fig. 1). To this end, this study aims to investigate the independent association of GDI and GII with mortality and incidence of the four major cancers of women.

2. Method

This is an ecological study to investigate the effect of gender inequality on the incidence and mortality of breast, ovarian, endometrial, and cervical cancer through two composite indices that capture it and compare them. The International Agency for Research on Cancer (IARC) reported data on the estimates of incidence and mortality of cancer in 2018 for 185 countries divided by gender and age group (Bray et al., 2018). Accordingly, the data on the number of new cases, the number of deaths due to cancer, and crude and Age-Standardized Rates (ASR) of incidence and mortality of cancer is freely accessible through the GOBOCAN database (Cancer IAfRo, 2020). The data on the incidence and mortality of female breast cancer, ovarian cancer, cervical cancer, and endometrial cancer were retrieved from the GOBOCAN 2018 database for 183 countries. Data on the Human Development Index (HDI) in 2018, the Gender Development Index (GDI) in 2018, and the Gender Inequality Index in 2018 were obtained from the United Nations Human Development Report (PROGRAMME).

The Institutional Review Board has approved this study. As we used freely available data on the web, no further ethical consideration was defined. No exclusion criteria were defined, and almost all of the countries for which there were estimates of incidence, mortality, HDI, GII, and GDI in 2018 were included in the final analysis.

Fig. 1 depicts the theoretical framework of this study. Disparities in development and unequal distribution of resources among countries partly account for the variations in different aspects of health. However, there are still many aspects of this disparity, particularly concerning women's health and other marginalized identities across countries and societies, that are frequently overlooked. In order to achieve equality that is inclusive and responsive, and which doesn't leave anyone behind, it is crucial to use intersectionality theory. Gender inequality is one of the most significant social factors to consider in addressing women's health disparities globally. To this end, many indices such as HDI, GII, and GDI are introduced to capture disparities among different countries, societies, and sectors.

HDI, an index to quantify the level of human development, is a number between zero and one and is based on three key dimensions: health (life expectancy at birth), education (years of schooling), and standard of living (Gross National Income per capita). According to HDI, countries fall into four categories, as follows: very high HDI (HDI $\geq$ 0.9), high HDI (HDI $\geq$ 0.8), medium HDI countries (0.8> HDI> 0.5), and low HDI (HDI$\leq$0.5) (UNDP, 2019). GDI was introduced in 1995 to measure gender disparities in the HDI. In a specific population, the ratio of HDI in females to HDI in males is the value of GDI. The closer the ratio is to one, the smaller the gap between females and males regarding human development. The GDI shows how much women lag behind their male counterparts and how much women need to catch up within each dimension of human development. The GII is another composite index of gender inequality estimated using three dimensions: reproductive health, empowerment, and the labor market. A low GII number suggests less disparity between men and women and vice versa. Therefore, the same estimated values of GII and GDI convey messages that are opposite to each other. It's worth noting that GII uses dimensions different from HDI. As a result, GII is not considered a measure of HDI loss and is treated as a separate index. On the other hand, GDI is closely linked to HDI and is often seen as an extension of it (UNDP, 2019).

While both indices aim to measure gender inequality, the GII specifically focuses on the loss of development due to gender inequality within a country, whereas the GDI measures gender inequalities in achievement in three basic dimensions of human development (Nationsa; Nationsb). Additionally, the GII is a composite index considering multiple dimensions of gender inequality, such as reproductive health, empowerment, and labor market participation. In contrast, the GDI is based on the ratio of female and male values of the HDI. the GII and GDI differ in their focus, dimensions, index composition, within-country variation, and measurement approach (Nationsa; Nationsb). Moreover, UNDP indices like the Gender Inequality Index are not appropriate to capture gender inequalities in highly developed countries like Europe due to vanished or reversed gender gaps in health, education, and parliamentary representation (Permanyer, 2013). Furthermore, it has also been shown that Low levels of human development are typically associated with disadvantages for girls and women (mostly due to education). In contrast, high levels are typically associated with disadvantages for boys and men (mostly due to shorter healthy life spans) (Stoet & Geary, 2019). Consequently, It also has been shown that GDI is a better index to capture gender inequality in highly developed countries when we want to investigate women's disadvantage (Stoet & Geary, 2019).

2.1. Data preparation and statistical analysis

In this study, we ranked countries based on their GDI and GII values in 2018. Quantiles of GDI and GII were defined and labeled as low (L) (1st quantile), low-middle (LM) (2nd quantile), middle (M) (3rd quantile), middle-high (MH) (4th quantile), and high (H) (5th quantile).

First, two univariate models were applied to investigate the relationship between GDI and GII indices with the incidence and mortality of each cancer. Then, Poisson regression modeling was applied. For each cancer, two models were fitted separately for each index of gender disparity (GDI and GII), including one for incidence and one for mortality. The ASR of incidence and mortality was defined as the outcome variable in each model. The level of gender inequality (GDI or GII) and HDI were considered the independent variables in the modeling of ASR of incidence of each cancer. In addition to the aforementioned variables, the ASR of incidence of each cancer was also considered as a predictor of the ASR of mortality of that cancer. HDI was applied in each model since the effect of this factor on mortality and incidence of these cancers was shown in previous studies, and we wanted to omit its impact.

To compare the ASR of incidence and mortality in regions with low GDI or GII with other regions, we estimated crude and adjusted incidence rate ratio (IRR) and its 95 % confidence interval (CI). A two-sided P-value of less than 0.05 was defined as a statistically significant level. Statistical analyses were performed using Stata (Release 11, College

Station, TX: Stata Corp LLC).

3. Results

Fig. 2 depicts the distribution of the ASR of incidence and mortality of each cancer in 2018. As shown, the distribution of incidence and mortality of these cancers vary widely across the countries. For instance, the highest ASR of BC incidence in 2018 was 24.3-fold of the lowest and the highest ASR of BC mortality was 15.8-fold of the lowest one.

3.1. GDI

Evaluating the role of GDI on the incidence and mortality of the cancers mentioned earlier, data on the GDI, available for 153 regions, was reviewed. The highest and lowest GDI in 2018 was observed in Barbados (GDI = 1.03) and Yemen (GDI = 0.5), respectively. Moreover, most countries are distributed within the GDI of 0.80–1.02. Only four countries had a GDI lower than 0.8, including Yemen (0.5), Afghanistan (0.71), Pakistan (0.76), and Chad (0.76), while five countries showed a GDI higher than 1.02 (Qatar, Estonia, Mongolia, Latvia, and Barbados). (Fig. 3).

According to the univariate models of GDI (Fig. 4), Incidence of breast, ovarian, and endometrial cancers started with high incidence in regions with low GDI and began to decrease as the GDI continued to rise to 0.75–0.8. After reaching regions with a GDI of 0.75–0.8, increasing trends were observed in the incidence of all aforementioned cancers with the rise of the GDI and the highest incidence was observed in regions with the highest GDI. In the case of the incidence of cervical cancer, an opposite trend to that of the other cancers was observed, and the highest incidence of this cancer was observed in regions with a GDI of 0.8.

Mortality of all cancers except for CC showed a relatively stable trend with the increase of the GDI. However, the lowest mortality of CC was observed when GDI was the lowest; as the GDI continued to rise to 0.8, the mortality began to rise and then decreased with more increases in the GDI, which was similar to its incidence trend.

According to the multivariable models (Table 1), GDI showed a non-linear association with the incidence of BC. All Regions, from regions with low-middle GDI to those with high GDI, showed a lower incidence of BC compared to that of regions with low GDI [0.65 ($P < 0.05$; 95 % CI: 0.59, 0.72) to 0.76 ($P < 0.05$; 95 % CI: 0.68, 0.84) of the incidence in regions with low GDI, respectively]. Additionally, only regions with low-middle GDI had lower mortality than regions with low GDI (IRR = 0.78, $P < 0.05$; 95 % CI: 0.67, 0.92), while other regions did not show any significant relationship.

GDI was not independently associated with the incidence of OC. However, regions with middle (IRR = 1.77, $P < 0.05$; 95 % CI: 1.08, 2.90) or high (IRR = 1.80, $P < 0.05$; 95 % CI: 1.09, 2.98) GDI showed higher mortality than regions with low GDI.

The incidence of CC was independently associated with the GDI, as regions with higher GDI had a higher incidence of CC. Accordingly, CC incidence in regions with high GDI was 2.89 ($P < 0.05$; 95 % CI: 2.48, 3.37) times higher than in regions with low GDI. Mortality of CC in regions with middle (IRR = 1.23, $P < 0.05$; 95 % CI: 1.00, 1.51) or high (IRR = 1.27, $P < 0.05$; 95 % CI: 1.01, 1.60) GDI was significantly higher than regions with low GDI while this was not the case for two remaining regions.

GDI was also independently associated with the incidence of EC and showed higher incidence in regions with middle to high GDI. However, the incidence in regions with low-middle GDI was not different from regions with low GDI (IRR = 1.22, $P > 0.05$; 95 % CI: 0.93, 1.60). Mortality of endometrial cancer in regions with low GDI was

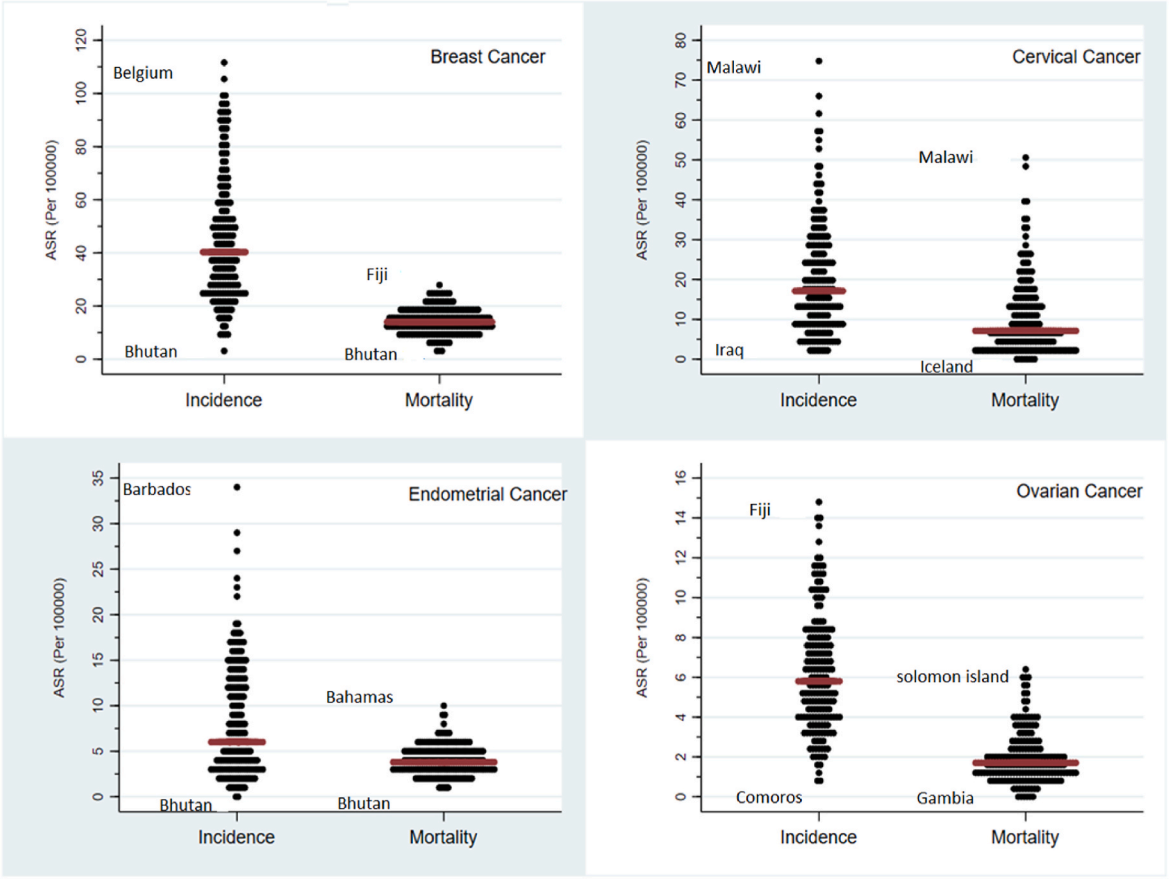

Fig. 2. Distribution of Incidence and mortality of Different Females Cancers across the Globe.

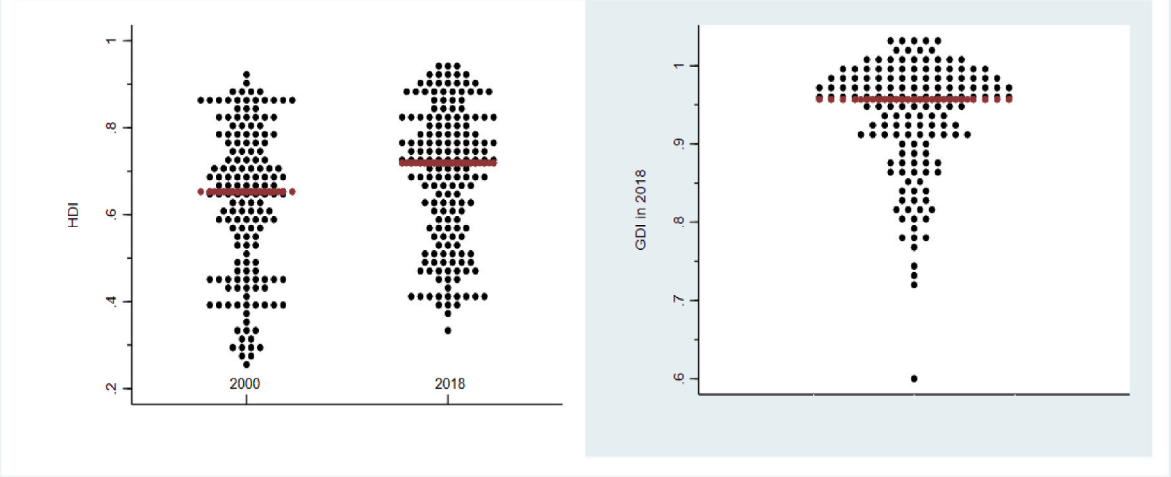

Fig. 3. Distribution of human development index (HDI) and gender development index (GDI) of different countries across the globe.

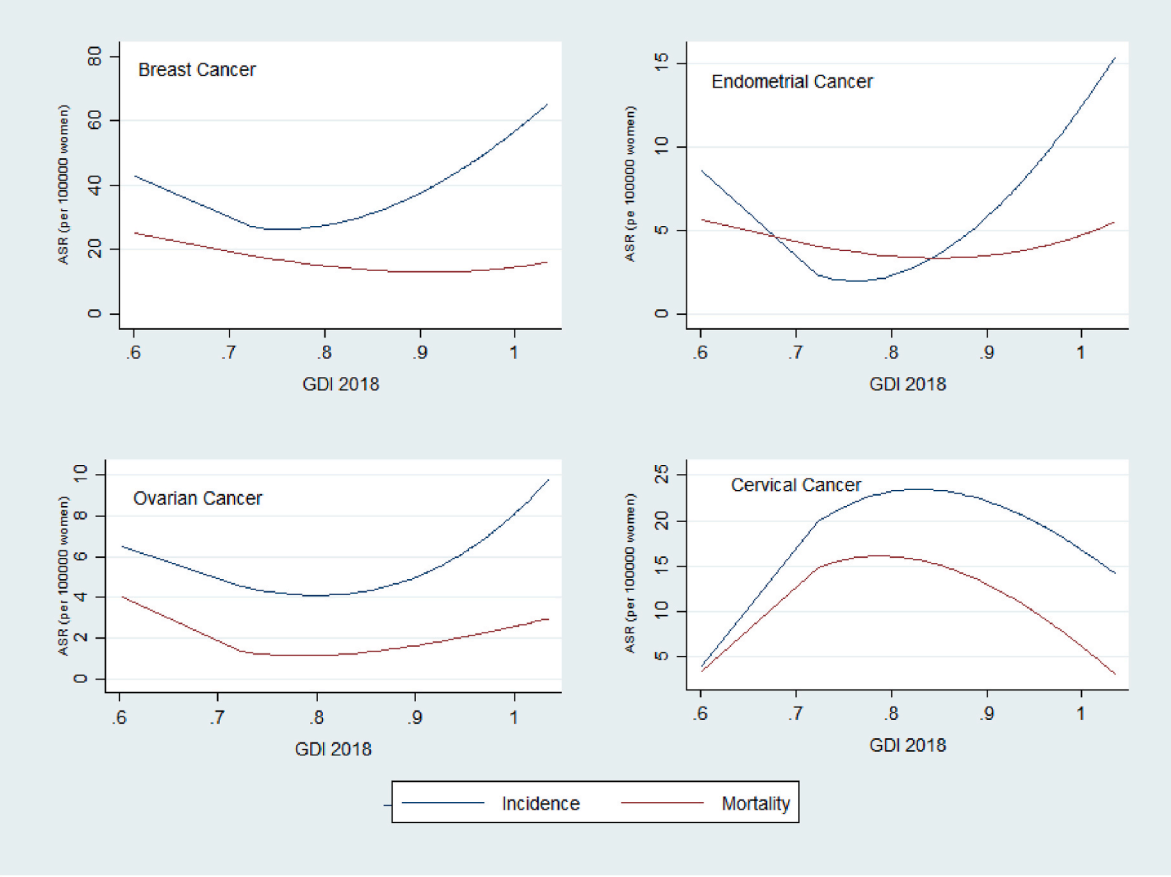

Fig. 4. Correlation of age-standardized incidence and mortality rate (ASR) of the females' cancers with gender development index (GDI).

significantly higher than in regions with middle GDI (IRR = 0.67, P < 0.05; 95 % CI: 0.48, 0.93).

3.2. GII

To evaluate the role of GII on the incidence and mortality of discussed cancers, data on the GII, which was available for 170 regions, was reviewed. The highest and lowest GII in 2018 was observed in Yemen (GII = 0.806) and Norway (GII = 0.018), respectively.

According to univariate models of GII (Fig. 5), the incidence of breast, ovarian, and endometrial cancers was highest when GII was low and began to decrease as the GII continued to rise. In contrast, the Incidence of cervical cancer showed a direct relationship with GII, and the highest incidence was observed in regions with the highest GII. Mortality of CC and BC showed an increasing trend with the increase of the GII. However, the Mortality of OC and EC showed a decreasing or relatively stable trend with the rise of the GII.

According to the multivariable modeling (Table 1), GII had a weak association with the incidence of BC; The incidence of BC only in regions with low-middle GII and middle GII were 0.82 (P < 0.001; 95 % CI: 0.76,

Table 1
Adjusted association of the GDI and GII with the incidence and mortality of Female Breast, Ovarian, Cervical, and Endometrial Cancers; *: a significant relationship.

Type of cancer	Outcome	Countries quantile	GDI Adjusted RR (95 % CI)	GII Adjusted RR (95 % CI)
Breast Cancer	Incidence (ASR)	LM	0.65 (0.59, 0.72) *	0.82 (0.76, 0.88) *
		M	0.71 (0.65, 0.79) *	0.82 (0.75, 0.90) *
		MH	0.78 (0.70, 0.86) *	0.93 (0.83, 1.05)
		H	0.76 (0.68, 0.84) *	1.05 (0.88, 1.24)
	Mortality (ASR)	LM	0.78 (0.67, 0.92) *	1.50 (1.28, 1.76) *
		M	0.84 (0.70, 1.01)	1.58 (1.31, 1.89) *
		MH	0.84 (0.70, 1.01)	1.43 (1.14, 1.78) *
		H	0.95 (0.79, 1.13)	1.42 (1.05, 1.91) *
Ovarian Cancer	Incidence (ASR)	LM	0.82 (0.63, 1.05)	1.03 (0.87, 1.23)
		M	0.81 (0.61, 1.06)	0.74 (0.61, 0.89) *
		MH	0.97 (0.73, 1.30)	0.69 (0.57, 0.83) *
		H	1.05 (0.81, 1.38)	0.52 (0.42, 0.64) *
	Mortality (ASR)	LM	1.23 (0.78, 1.95)	0.98 (0.77, 1.25)
		M	1.77 (1.08, 2.90) *	1.08 (0.84, 1.40)
		MH	1.59 (0.92, 2.73)	1.20 (0.93, 1.56)
		H	1.80 (1.09, 2.98) *	1.26 (0.95, 1.68)
Cervical Cancer	Incidence (ASR)	LM	2.03 (1.81, 2.28) *	1.08 (0.92, 1.27)
		M	2.49 (2.16, 2.87) *	1.29 (1.09, 1.53) *
		MH	2.70 (2.26, 3.21) *	1.27 (1.04, 1.56) *
		H	2.89 (2.48, 3.37) *	1.02 (0.79, 1.32)
	Mortality (ASR)	LM	0.91 (0.76, 1.08)	1.47 (1.11, 1.95) *
		M	1.23 (1.00, 1.51) *	2.00 (1.51, 2.65) *
		MH	1.22 (0.93, 1.60)	1.85 (1.34, 2.55) *
		H	1.27 (1.01, 1.60) *	1.81 (1.25, 2.61) *
Endometrial Cancer	Incidence (ASR)	LM	1.22 (0.93, 1.60)	0.99 (0.84, 1.17)
		M	1.72 (1.32, 2.25) *	0.74 (0.60, 0.93) *
		MH	1.69 (1.27, 2.25) *	0.46 (0.34, 0.63) *
		H	2.12 (1.62, 2.78) *	0.50 (0.32, 0.78) *
	Mortality (ASR)	LM	0.78 (0.58, 1.04)	1.42 (1.02, 1.98) *
		M	0.67 (0.48, 0.93) *	1.70 (1.18, 2.46) *
		MH	0.78 (0.55, 1.12)	1.52 (0.95, 2.44)
		H	0.82 (0.58, 1.16)	1.91 (1.19, 3.05) *

0.88), and 0.82 ($P < 0.001$; 95 % CI: 0.75, 0.9) of incidence in regions with low GII, respectively. However, GII in this model showed a non-linear association with BC mortality, and regions with a low-middle GII to high GII all had higher mortality than regions with low GII (Table 1).

Incidence of OC was independently associated with the GII, showing lower incidence in countries with Higher GII (IRR = 0.52, $P < 0.001$; 95 % CI: 0.42, 0.64). However, GII was not significantly associated with the mortality of OC in other regions compared to regions with low GII.

Incidence of CC was only associated with GII in middle and high-middle GII regions, which shows 1.29 ($P = 0.003$; 95 % CI: 1.09, 1.53) and 1.27 ($P = 0.019$; 95 % CI: 1.04, 1.56) higher incidence of CC compared to low GII regions. Mortality of CC was independently associated with the GII, as regions with higher GII had higher mortality of CC. CC mortality in regions with high GII was 1.85 ($P < 0.001$; 95 % CI: 1.25, 2.61) times higher than in regions with low GII.

GII was also independently associated with the incidence of EC and showed a lower incidence of EC in regions with higher GII (IRR = 0.50, $P = 0.002$; 95 % CI: 0.32, 0.78). However, the incidence in regions with a low-middle GII was not significantly different from regions with low GII (IRR = 0.99, $P = 0.939$; 95 % CI: 0.84, 1.17). Similarly, Mortality of endometrial cancer was independently associated with GII, except in regions with middle-high GII. As a result, the mortality of EC in high GII regions was 1.91 ($P = 0.007$; 95 %CI: 1.19, 3.05) times higher than that of low GII regions.

4. Discussion

In this study, we found that gender inequality, one of the social determinants of health and a barrier to reaching "Health for All," is an influential determinant of the incidence and mortality of cancers among women. In line with unequal distribution and access, the theoretical and conceptual basis for this finding is supported by the notion that gender inequality, which is reflected in lower levels of education and economic independence of women, can contribute to an increased risk of cancer, less access to cancer screening and treatment, and delay in diagnosis and treatment, thus poorer health outcomes. Furthermore, another finding of this study was that both GDI and GII have their pros and cons in capturing the effect of gender inequality on the incidence and mortality of breast and gynecological cancer. Interestingly, we also found that after adjusting the models with the HDI level of different countries, the former associations of GDI and GII with the incidence and mortality of these cancers changed.

Overall, we expected with the increase in gender inequality, the incidence of BC, OC, CC, and EC would increase due to the increase in exposure to risk factors associated with these cancers, specifically regarding cervical cancer and lower vaccination coverage against human papillomavirus (de Martel et al., 2020; Gakidou et al., 2008). At the same time, we also considered the decrease in incidence due to under-diagnosis or under-reporting (Bray et al., 2012, 2018). Regarding mortality of women's cancers, we hypothesized that this outcome would increase with the increase of gender inequality due to lack of awareness and screening protocols, limited or no access to diagnostic centers in rural areas for early detection, and lower standards of healthcare facilities (Cusimano et al., 2019; Francies et al., 2020; Paneru et al., 2023; Reid et al., 2017). However, underdiagnosis and underreporting of the cause of death in less developed countries because of Limited resources, Lack of standardized reporting, Cultural and social factors like discussing death being taboo, and censorship due to political factors can completely alter this association (Dattani & Roser, 2023).

According to univariate model findings, the association of GDI with the incidence of women's cancers showed a relatively similar trend to that of HDI (Hu et al., 2016; Martínez-Mesa et al., 2017; Singh et al., 2012), provided that we exclude the effect of the four mentioned countries with GDI less than 0.8. However, the association of GII with the incidence of these cancers showed an opposite trend to that of HDI and GDI (Hu et al., 2016; Martínez-Mesa et al., 2017; Singh et al., 2012). Moreover, the association of GDI with the mortality of breast and cervical cancers showed a relatively similar trend to that of HDI. In contrast, the mortality of OC and EC showed different relationships with

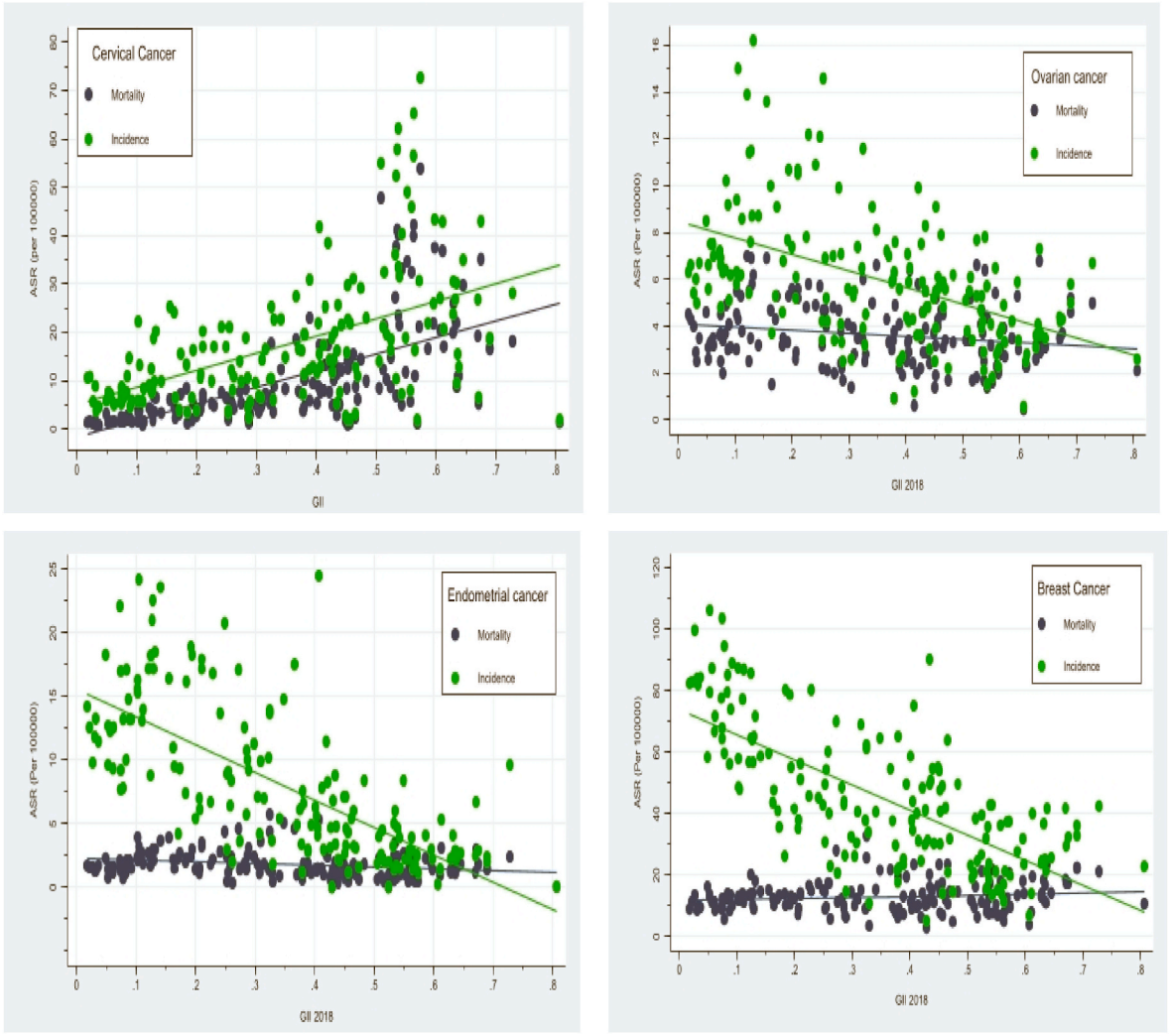

Fig. 5. Correlation of age-standardized incidence and mortality rate (ASR) of the females' cancers with gender inequality index (GII).

GDI compared to their relationships with HDI (Hu et al., 2016; Martínez-Mesa et al., 2017; Singh et al., 2012). However, the association of GII with the mortality of these cancers showed an opposite trend to that of HDI and GDI (Hu et al., 2016; Martínez-Mesa et al., 2017; Singh et al., 2012). Accordingly, removing the effects of HDI in multivariable models resulted in a completely different correlation in each cancer model.

4.1. Breast cancer

The association of GDI and GII with the BC incidence was incongruent. The higher rate of BC incidence in countries with lower GDI can be explained by the higher prevalence of risk factors associated with BC, which are unrelated to the HDI and its components in these countries. One of these risk factors might be the less opportunity for women to be physically active in countries with lower GDI (Moreno-Llamas et al., 2022). Consequently, this can result in a higher prevalence of obesity, a known risk factor of BC (Francies et al., 2020), among women in such regions compared with countries with higher GDI, where women have more opportunities for healthier lifestyles (Moreno-Llamas et al., 2022). Moreover, women in countries with low GDI have a higher risk of exposure to particular oral contraceptives compared with countries with high GDI (Francies et al., 2020; Kanadys et al., 2021). On the other hand, women's higher awareness, access, and utilization of advanced diagnostic technologies as indicated by lower GII, and the difference in incidence rates of BC by more than 10-fold among selected registries in developed countries and less developed ones (Francies et al., 2020), can explain the higher incidence of BC in more egalitarian countries with low GII and consequently an artificially lower incidence in countries with higher Gender inequality (Kish et al., 2014; Martínez-Mesa et al., 2017). In addition, higher BC mortality in less egalitarian countries found in the GII model can be explained by a higher rate of late diagnosis, less access and utilization of cancer treatment like radiotherapy, less social support, and other cultural issues such as the stigmatization of BC in these countries (Kish et al., 2014; Okojie, 1994).

4.2. Ovarian cancer

In the GII model, the incidence of OC was lower in countries with higher Gender inequality. However, this finding might be artificial and should be interpreted with more caution. It is rational to think that some risk factors of OC, such as obesity and lower access to contraceptive methods (Reid et al., 2017), are more prevalent in countries with higher gender inequality than in more gender-equal countries where the chance of diagnosis and reporting of OC is higher, a situation in which a higher risk of OC could be compromised with the higher probability of diagnosis and reporting of OC (Reid et al., 2017). Moreover, GDI was positively correlated with the mortality of OC. We also believe that this finding might be artificial which is explainable by the higher quality of female death reports in countries with higher GDI (Dattani & Roser, 2023; Reid et al., 2017). Timely diagnosis and more advanced

therapeutic technologies, which are primarily available and utilized by women living in countries with higher GDI, decrease cancer mortality in these countries (Reid et al., 2017). However, we should also consider that sudden economic growth and lifestyle changes have been shown to be associated with sudden increases in both incidence and mortality rates of OC in historically less developed countries. Therefore, to explain this finding, besides the fact of under-reporting of both incidence and mortality of OC in less gender-equal countries, there might also be a risk factor correlated to OC which is prevalent in more gender-equal countries, such as a lower rate of pregnancy and higher life expectancy of women (Reid et al., 2017).

4.3. Cervical cancer

While the GDI model indicates the increase in incidence in more gender-equal societies, the GII model shows less incidence of CC in these societies. Also, this association of GDI is not in line with a similar study using GII by Singh et al. (Singh et al., 2012). This discrepancy could be because Singh et al. did not adjust the data for the effect of HDI. However, our GII model result was congruent with this study in middle and middle-high countries. Considering the higher risk of CC in low-middle income countries -mostly with lower GDI- as a result of little to no vaccination against HPV and lack of access to CC screening (Bray et al., 2018; de Martel et al., 2020; Singh et al., 2012), under-diagnosis and under-reporting of incidence of CC may be the most rational explanation for this finding in low GDI countries. In addition, more stigmatization of CC in countries with lower GDI, which is associated with a significant drop in CC screening uptake among women residing in these countries (Paneru et al., 2023; Peterson et al., 2021), alongside the fact that only 19 % of women in developing countries have access to screening tests compared to 63 % in developed countries (Gakidou et al., 2008) can lead to underdiagnosis and underreporting of the CC in less gender-equal countries.

Similar to CC incidence models, both GDI and GII were positively correlated with CC mortality, thus conveying incongruent signals. In the case of the direct association of CC mortality with GDI, which might be an artificial finding, again, the obvious difference between the quality of cause-of-death reports and death registries in countries is the most plausible explanation (Dattani & Roser, 2023). Conversely, reasons for higher mortality of CC in less gender-equal countries in the GII model can be limited access to healthcare and cervical cancer screening in low- and middle-income countries, fear of death associated with a positive HPV test, and cultural beliefs that stigmatize reproductive health issues and consider discussing them a taboo (Hull et al., 2020; Lin et al., 2021). Ginjupalli et al. showed that Fear of death, which stems from a lack of understanding of the differences between HPV and cervical cancer, and Discriminatory attitudes of community members, including assumptions of promiscuity, infidelity, or HIV status, prevent women from accessing screening and treatment opportunities which can be addressed by increasing the awareness of HPV (Ginjupalli et al., 2022).

4.4. Endometrial cancer

Both multivariable models showed that the incidence of EC was higher in more gender-equal countries. This association might be due to a lack of knowledge about abnormal uterine bleeding, stigmatization of endometrial cancer, and its symptoms in countries with lower gender equality, which can lead to less utilization of services related to EC diagnosis and eventually underdiagnosis of this cancer (Cusimano et al., 2019). Moreover, the similar correlations between gender equality level and incidence of cervical and uterine malignancies can be explained by their common heralding sign, vaginal bleeding, and requirement of gynecological exam for diagnosis. Because this sign and discussion of menstruation are considered taboo in less egalitarian countries, patients may not seek medical care due to lack of knowledge, fear of testing, and stigmatization (Jia et al., 2013), contributing to under-diagnosis of CC and EC (Olson et al., 2022; Paneru et al., 2023). Consequently, higher mortality of EC in less gender-equal countries could be explained by a lack of knowledge about abnormal uterine bleeding and menstruation, the prohibition of education about reproductive health issues, and the stigmatization of endometrial cancer symptoms in countries with lower gender equality (Cusimano et al., 2019). Moreover, more aggressive histology in black women, limited access to healthcare leading to Advanced stage at diagnosis, and lower chance to receive definitive surgical treatment and radio/chemotherapy increase mortality of EC in less gender-equal societies (Whetstone et al., 2022).

Prior to our research, there was a dearth of studies that mentioned the relationship between gender inequality and the elevated rates of incidence and mortality of cervical, ovarian, endometrial, and breast cancers (Benigni, 2007; Veas et al., 2021). In addition, studies have demonstrated that gender inequality can be related to disparities in all cancer incidence and mortality rates between nations (Torre et al., 2017). A study by Singh et al. (Singh et al., 2012) found that women in countries with high gender inequality had higher rates of cervical cancer incidence and mortality compared to women in more gender-equal countries. Additionally, a study by Torre et al. (Torre et al., 2017) reported that gender inequality was associated with higher rates of lung cancer mortality among women. These findings highlight the importance of understanding the relationship between gender inequality and cancer incidence/mortality and the need for interventions aimed at addressing gender disparities in health outcomes of women's cancer.

Generally, studies have shown that gender inequality is a major determinant of health outcomes, particularly for women. A study conducted in India found that gender-based discrimination in the health sector led to adverse health outcomes for women, including higher maternal mortality rates, lower life expectancy, and increased vulnerability to sexually transmitted infections (STIs) (World Health Organization, 2021). Similarly, research in Bangladesh demonstrated that gender inequality in education and employment opportunities limited women's access to health care, resulting in higher rates of maternal and child mortality (Anwar et al., 2015). To better understand and address gender-based health inequalities, Studies have shown that gender inequality in education, employment, and income can limit women's access to healthcare services and contribute to poorer health outcomes (Health CoSDo, 2008; Marmot, 2005). Moreover, women in patriarchal societies may experience discrimination in the healthcare system, resulting in poor health outcomes (Krieger, 2003). Sen and Östlin (Sen & Östlin, 2008) note that gender-based inequalities in education can limit women's knowledge about health and their ability to access healthcare services. Krieger (Krieger, 2003) similarly argues that social structures that contribute to gender-based inequalities, such as sexism and gender discrimination, can lead to poorer health outcomes for women. In contrast, Studies have shown that Gender Development is associated with better health outcomes for women, including lower maternal mortality rates and higher life expectancies (Grown et al., 2005; Paul et al., 2022; UNDP, 2019). Despite these findings, there are still significant research gaps in understanding the complex relationships between gender inequality and health. For instance, gender is one aspect of marginalization in intersectionality theory. Therefore, Conducting a comprehensive investigation into the multifaceted dimensions of gender inequality and its intersection with other societal factors, that contribute to the stratification of women, is essential in gaining a deeper understanding of how gender inequality influences women's health. (Women UNEfGEatEoWU and Kabir, 2021). Furthermore, the role of gender and masculinity in shaping men's health outcomes is an area that requires further investigation (Courtenay, 2000). while previous studies have shown a link between gender inequality and health disparities, to better address gender-based health disparities there is a need for more in-depth research to understand the different relationships and mechanisms through which gender inequality in contribution to other intersecting identities impacts different health outcomes of women in various contexts (Krieger, 2003; Women UNEfGEatEoWU and Kabir, 2021).

Addressing gender-based health disparities requires comprehensive Gender-sensitive approaches, which consider particular healthcare needs while addressing the causes of gender-based health inequities and ways to transform harmful gender norms, roles, and relations while focusing on promoting gender equality (Celik et al., 2011). This includes efforts to improve women's education (Paul et al., 2022) and economic opportunities (Grown et al., 2005), as well as addressing gender discrimination and other structural factors that contribute to gender-based inequalities (Sen & Östlin, 2008; Weitzman, 2017). It has been shown that education, increasing health literacy, and empowerment of women can contribute to increased utilization of healthcare services, which can ultimately lead to better health outcomes (Shen et al., 2019). Specifically, studies have shown that educating and removing the stigma surrounding menstrual and reproductive health can help increase awareness, which can ultimately lead to timely diagnosis of gynecological cancer and better gynecological health outcomes (Olson et al., 2022). In addition, promoting gender equality through increased economic opportunities for women has been associated with improved health outcomes, including reduced maternal mortality rates and increased access to healthcare services (Bauer, 2014; Vohra-Gupta et al., 2023).

Regarding addressing gender disparities in health outcomes of women's cancer, studies have shown that simple measures like spreading the knowledge about the prevention and importance of screening for women's cancer through traditional healers (Nelson et al., 2010) or integrating health messages with marriage counseling (Kapambwe et al., 2013) can significantly improve health outcomes. These studies align with our findings because these initiatives improved Gender equality, resulting in better prevention, timely diagnosis, and treatment. Therefore, thorough targeting of women's education focusing on health literacy, specifically reproductive and menstrual health (Olson et al., 2022) and accessibility of health care system for women focusing on the independence of women and expanding health care coverage (Cardoso et al., 2021), Gender-sensitive approaches (Celik et al., 2011), and overcoming language and cultural barriers (Olson et al., 2022), policymakers can adopt intersectionality approach to design interventions that aim to reduce gender inequality and improve women's health outcomes (Vohra-Gupta et al., 2023), thus reducing the incidence and mortality of cervical, ovarian, endometrial, and breast cancer.

Our findings highlight the need for policies that promote gender equality and empower women through education and economic opportunities. Policymakers can use the GDI, GII, and their components, particularly those related to education and health, to track progress toward gender equality and to identify areas where interventions are needed to reduce gender disparities in cancer outcomes (Bauer, 2014; Vohra-Gupta et al., 2023). By focusing on education and economic participation, policymakers can design interventions that aim to reduce gender inequality and improve women's health outcomes, including reducing the burden, incidence, and mortality of cervical, ovarian, endometrial, and breast cancers. Accordingly, meaningful change in gender inequality requires fundamental actions over a relatively long period, and its sudden improvement is unlikely. However, this is not the case for its worsening, which can happen so suddenly when women are systematically deprived of their fundamental rights, which directly excludes them from society and the economy, thus reducing their autonomy, as is the case in Afghanistan. Bottom line, gender inequality is so important and universal that the UNDP's fifth Goal of the 2015–2030 SDGs is "GENDER EQUALITY," and healthcare policymakers should consider this social issue to reach "HEALTH FOR ALL" and "GOOD HEALTH AND WELL-BEING," the third goal of sustainable development (Sustainable development goals, 2015).

4.5. Limitations of this study

Although we used the most qualified available data on cancer incidence and mortality, HDI, GII, and GDI, significant differences in the quality and coverage of data used are the most challenging limitations of our study, particularly in some low- and middle-income countries. The availability and accuracy of data across countries may be subject to variations due to differences in definitions, methodologies, and data collection techniques employed by respective national registries and databases. As a result, estimates derived from such data may lack precision and fail to provide a wholly representative picture.

The second limitation of this study pertains to its ecological nature and requires careful consideration when interpreting the results to avoid an ecological fallacy. Thus, it is imperative to avoid the attribution of group characteristics to individual members.

The third limitation of this study is the limitations of indices used to measure the level of gender inequalities. One limitation of GDI is that the earned income component may not be sensitive enough to capture the full extent of gender inequality, particularly in low-income countries. On the other hand, the GII has a limited number of indicators compared to the GDI, which may make it less useful in capturing the complex relationship between gender development and health outcomes. Additionally, both indices may not fully capture the intersectionality of gender with other social factors, such as race or ethnicity, which may impact cancer incidence and mortality differently. Nonetheless, both indices are still valuable tools for analyzing gender inequalities, especially about health outcomes.

5. Conclusions

This study revealed that Incidence and mortality of cancers among women are ecologically associated with the country-level gender inequality measured by GDI and GII. It can be inferred that the implementation of gender equality and relevant strategies within public health policies could potentially lead to a decrease in the number of cancer-related fatalities among women. Consequently, prioritizing policies and interventions that address gender disparities in healthcare access and outcomes may have the potential to improve cancer prevention, diagnosis, and treatment in female populations. It is crucial for public health professionals to prioritize gender equity in their efforts to reduce cancer mortality rates, as this may contribute to the development of more effective and equitable healthcare systems. Additionally, future studies are needed to identify and control gender-related issues that contribute to a lower quality of programs targeted at the prevention, screening, early detection, and treatment of cancers and other non-communicable diseases in women.

Declaration

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Ethical Statement for solid-state ionics

Hereby, I, Hossein Molavi Vardanjani, consciously assure that for the manuscript "Worldwide Association of the Gender Inequality with the Incidence and Mortality of Cervical, Ovarian, Endometrial, and Breast Cancers" the following is fulfilled.

1) This material is the authors' original work, which has not been previously published elsewhere.

2) The paper is not currently being considered for publication elsewhere.
3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
4) The paper properly credits the meaningful contributions of co-authors and co-researchers.
5) The results are appropriately placed in the context of prior and existing research.
6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper references.
7) All authors have been personally and actively involved in substantial work leading to the paper and will take public responsibility for its content.

I agree with the above statements and declare that this submission follows the policies of Solid State Ionics as outlined in the Guide for Authors and in the Ethical Statement.

CRediT authorship contribution statement

Shahin Kavousi: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Najmeh Maharlouei:** Conceptualization, Methodology, Writing – review & editing. **Alireza Rezvani:** Supervision, Writing – review & editing. **Hossein Akbari Aliabad:** Data curation, Writing – original draft. **Hossein Molavi Vardanjani:** Conceptualization, Formal analysis, Supervision, Writing – original draft, Writing – review & editing.

Data availability

we have used already online available data and the link to obtain data is mentioned in manuscript

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