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ORIGINAL RESEARCH

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The global incidence, mortality, and burden of uterine cancer in 2019 and correlation with SDI, tobacco, dietary risks, and metabolic risk factors: An ecological study

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Abstract

Background and Aim: Endometrial cancer (EC) is the sixth most common cancer among women worldwide. Since global studies are based on awareness of the incidence trend, mortality, geographical diversity, and level of social development and income of countries, this study was conducted to investigate the trend of uterine cancer (UC) in the world in 2019.

Methods: Age-standardized rates (ASR) of incidence, deaths, prevalence, and disability-adjusted life years (DALYs) of UC, as well as targeted risk factors, were extracted from the Global Burden of Disease (GBD) online database 2019. Pearson correlation coefficient and SPSS 16 were used to calculate the correlation between risk factors and ASR of epidemiological indicators. Statistical significance was considered as $p < 0.05$.

Results: In 2019, the age-specific incidence and death rate of UC was peaking at 60–64 and 65–69 years, respectively. The highest age-standardized incidence rate per 100,000 people for UC has been reported in the Northern Mariana Islands, high sociodemographic index (SDI) countries, World Bank High-Income category, Europe continent and among World Health Organization (WHO) regions were found in the European Region. The highest age-standardized death rate per 100,000 people for UC has been reported in Grenada, high SDI countries, the World Bank High-Income category, Europe continent, and among WHO regions found in the European Region. In 2019, the age-standardized DALYs rate was 53.54 per 100,000 inhabitants, of which 48.49 cases were related to years of life lost (YLLs) and 5.05 cases were related to years lived with disability.

Conclusion: According to GBD-2019, the highest incidence, mortality, and DALY of UC are in Europe. The evidence and traces of diversity can be seen in the inequalities of UC. Race, ethnicity, economic status, level of education and awareness, co-morbidities, access, grade, and histological type of tumor are the most important causes of this inequality.

KEYWORDS

burden, global, incidence, mortality, uterine cancer

1 | INTRODUCTION

Endometrial cancer (EC) is the sixth most common cancer among women all over the world, and its incidence has increased dramatically over the past two decades.[1] In 2019, a total of 435,041 new cases of EC were diagnosed and 91,641 related deaths occurred worldwide. Based on FIGO guidance, this cancer is classified into I, II, III, and IV stages reflecting the various histological types, tumor patterns, and molecular classification.[2] Early-stage disease is the most common disease, and its associated 5-year overall survival (OS) is 81%. However, the 5-year OS for stage IVA and IVB EC is only 17% and 15%, respectively.[3]

Genetic, reproductive, lifestyle, and anthropometric factors are associated with the occurrence of EC.[4] Although no effective screening method has yet been identified for this disease, approximately 70% of patients are diagnosed in the early stages of cancer. Therefore, the 5-year survival rate of this cancer is high.[5] Despite the favorable prognosis of EC, some patients still have a low survival rate, which is due to factors such as socioeconomic inequalities.

EC is mainly a postmenopausal disease and the average age of patients diagnosed with this cancer is 60 years.[5] The incidence of EC in premenopausal ages is between 14% and 20%.[6] Most of the young women with EC have more favorable histology with better prognosis, and are diagnosed in early stages of cancer with less involvement of myometrium and the absence of lymphatic vascular invasion.[6,7] Most patients seek treatment with symptoms such as postmenopausal bleeding or abnormal uterine bleeding, and in advanced stages, they may have pain, abdominal bloating, bowel and bladder dysfunction, premature fullness, dyspnea, and dyspareunia.[5]

Due to the fact that the awareness about the incidence trend, mortality, geographical diversity, and also the level of social development and the income of countries are basis for global studies, this study was conducted with the aim of investigating the trend of EC in the world in 2019.

2 | METHODS

Uterine cancer (UC) was defined according to the International Classification of Diseases (ICD)-10 codes as C55, as well as according to the ICD-9 code as 182.0.

2.1 | Data sources

Age-standardized rates (ASR) of incidence, deaths, prevalence, and disability-adjusted life years (DALYs) of UC, as well as targeted risk factors, were extracted from Global Burden of Disease (GBD) online database 2019, which presented the latest data for disease epidemiology indexes at http://ghdx.healthdata.org. In GBD, epidemiologic indicators for 369 illnesses and injuries for both sexes in 204 countries and territories based on different country divisions have been estimated.

For a precise interpretation, EC data have been extracted for 204 countries and a variety of classifications based on age groups, sociodemographic index (SDI), World Health Organization (WHO) regions, continents, World Bank regions, and GBD regions.[8–10] The SDI identifies the position of countries or geographical areas on a development scale ranging from zero (minimum) to one (maximum); and is the geometric mean of three factors, including income per capita, the average number of years of education, and the overall fertility rate.[11]

The World Bank (WB) classifies economies for analysis according to four income groups (low, lower-middle, upper-middle, and high income). For this purpose, it uses data on per capita gross national income in the United States (US) dollars converted into local currency, using the World Bank's Atlas methodology, which is applied to smooth exchange rate fluctuations.[12]

In GBD, the developed internationally standardized form of quality-adjusted life years was defined as DALYs and is equal to the summation of the years of life lost (YLL) due to premature death and the years lived with a disability of specified severity and duration.[10]

2.2 | Definitions

In GBD 2019, high body mass index (BMI) was defined as adults (age 20+ years) with BMI ≥ 25 kg/m^2 and using thresholds from the International Obesity Task Force standards for children (aged <20 years).[13]

In GBD, metabolic risks included high fasting plasma glucose (FPG), high low-density lipoprotein (LDL) cholesterol, high systolic blood pressure (SBP), high BMI, low bone mineral density (BMD), and kidney dysfunction. In previous meta-analysis studies, the minimum level of death or DALY-weighted multicause risk factor curves is defined to be the theoretical level of exposure to the minimum risk of one specific risk factor.[13,14]

High FPG levels are defined as any level above 4.8–5.4 mmol/L,[15] high LDL cholesterol levels are defined as LDL-cholesterol levels above 0.7–1.3 mmol/L,[16] and high SBP levels are defined as SBP levels above 110–115 mmHg.[17]

In the staging criteria for acute kidney injury classification (CKD stages 1–5), the definition of kidney dysfunction was based on urinary albumin to creatinine ratio and estimated glomerular filtration rate.[18]

Based on the NHANES study, the 99th percentile of BMD by age and sex was determined to be the TMREL of low BMD due to variations in bone mineral content.[13]

In GBD 15 dietary risk factors have been investigated. We selected seven of these risk factors that we thought were associated with UC. In GBD study, diet low in vegetables has been defined as the mean daily consumption of vegetables (fresh, frozen, cooked, canned, or dried vegetables, excluding legumes and salted or pickled vegetables, juices, nuts, seeds, and starchy vegetables such as potatoes or corn) with the Optimal level of intake 360 g/day. Diet low in whole grains has been defined as the Mean daily consumption of whole grains (bran, germ, and endosperm in their natural proportion) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes, and other sources with the optimal level of intake 125 g/day. Diet low in fruits has been defined as the mean daily consumption of fruits (fresh, frozen, cooked, canned, or dried fruits, excluding fruit juices and salted or pickled fruits) with the optimal level of intake equal to 250 g/day.[19–23]

Also, diet high in red meat has been identified as the mean daily consumption of red meat (beef, pork, lamb, and goat, but excluding poultry, fish, eggs, and all processed meats) with the optimal level of intake between 0 gr and 14.3 gr per day. Diet high in processed meat has been identified as the mean daily consumption of meat preserved by smoking, curing, salting, or addition of chemical preservatives with the optimal level of intake equal to 2 g/day.[19–23]

Diet high in trans fatty acids has been identified as the Mean daily intake of trans fat from all sources, mainly partially hydrogenated vegetable oils and ruminant products with the optimal level of intake equal to 0.5% of total daily energy. Diet low in calcium has been defined as the mean daily intake of calcium from all sources, including milk, yogurt, and cheese with the optimal level of intake equal to 1.25 g/day.[19–23]

2.3 | Statistical analysis

The ASR of incidence, deaths, prevalence, and DALYs were expressed as numbers per 100,000 populations and with a 95% confidence interval (CI) for the different classification's description. The influence of different ages in the patient population was removed by using ASRs in figures per 100,000 populations. Pearson correlation coefficient and SPSS 16 were used to calculate the correlation between chewing tobacco, diet low in vegetables, diet low in whole grains, diet high in processed meat, diet high in trans fatty acids, high fasting plasma glucose, and high BMI and age-standardized incident rates, death rates, and DALYs rates of UC. Statistical significance was considered as $p < 0.05$. Definitions used in this study can be found at https://www.healthdata.org/terms-defined and https://www.healthdata.org/gbd/.[10]

3 | RESULTS

3.1 | Global age-specific distribution of UC

In 2019, the age-specific incidence of UC was peaking at 60–64 years with 72,318 (95% CI: 65,593–79,605) new cases. Age-specific death counts were peaking at 65–69 years with 14,335 (95% CI: 13,125–16,017) death, respectively. Also, most DALYs counts were recorded in 50-54 years with 387,230 (95% CI: 34,8301–429,782) (Figure 1).

3.2 | Incidence of UC

A total of 435,041 (95% CI: 397,021–479,729) new cases of UC were reported worldwide in 2019, with an age-standardized incidence rate (ASIR) of 9.99 (95% CI: 9.12–11.02) per 100,000 populations.

The highest ASIR per 100,000 peoples for UC have been reported in Northern Mariana Islands (32.77), Russian Federation (32.55), Bulgaria (30.66), American Samoa (29.82), Grenada (29.41), Latvia (29.1), the US (28.8), Italy (26.93) and Cuba (26.49), respectively.

The lowest ASIR per 100,000 peoples for UC have been reported in Nigeria (2.83), Bangladesh (3.99), Palau (2.78), Yemen (3.38), Malawi (2.86), Kenya (3.19), Sudan (3.63), Nepal (5.38) and India (3.26), respectively.

Statistics show that the highest ASIR for UC occurs in countries with High SDI (19.16 per 100,000) and the lowest ASIR occurs in countries with Low SDI (4.43 per 100,000).

According to the World Bank classification, the ASIR for UC is highest in the high-income category (19.91 [95% CI: 17.81–22.17] per 100,000 population). The lowest rates were seen in low-income countries (4.43 [95% CI: 3.64–5.07] per 100,000 population).

Among the continents, the highest ASIR was reported in Europe, while the lowest was observed in Africa.

The highest ASIR for UC among WHO regions was found in the European Region (20.74 [95% CI: 18.62–23.14] per 100,000 population). The lowest was reported in the African region (3.35 [95% CI: 2.63–4.04] per 100,000).

In the GBD regions, the highest ASIR is seen in High-income North America (27.82 per 100,000) and then Eastern Europe (27.50 per 100,000) and the lowest in Western Sub-Saharan Africa (2.64 per 100,000). More details are presented in Table 1 and Figures 2, 3, and 4.

3.3 | Death of UC

In 2019, 91,641 (95% CI: 82,389–101,502) death due to UC was reported worldwide. The age-standardized death rate (ASDR) of UC worldwide was 2.09 (95% CI: 1.88–2.32) per 100,000 inhabitants.

The highest ASDR per 100,000 peoples for UC have been reported in Grenada (11.3), American Samoa (10.74), Saint Vincent and the Grenadines (8.08), Northern Mariana Islands (7.66), Barbados (7.55), Solomon Islands (7.53), Jamaica (7.04), Guyana (6.9), and Nauru (6.88), respectively.

The lowest ASDR per 100,000 peoples for UC have been reported in Palau (0.52), Algeria (0.75), the Republic of Korea (0.77), Nigeria (0.8), San Marino (0.83), Turkmenistan (0.91), Bangladesh (0.93), Iran (Islamic Republic of Iran) (0.98), and Yemen (0.98), respectively.

Statistics show that the highest ASDR for UC occurs in countries with High SDI (2.52 per 100,000). The lowest ASDR occurs in countries with Middle SDI (1.61 per 100,000).

According to the World Bank classification, the ASDR for UC is highest in the World Bank High-Income category (2.62 [95% CI: 2.42–2.75] per 100,000 population). The lowest rates were seen in World Bank Upper Middle-Income countries (1.78 (95% CI: 1.56-2.08) per 100,000 population).

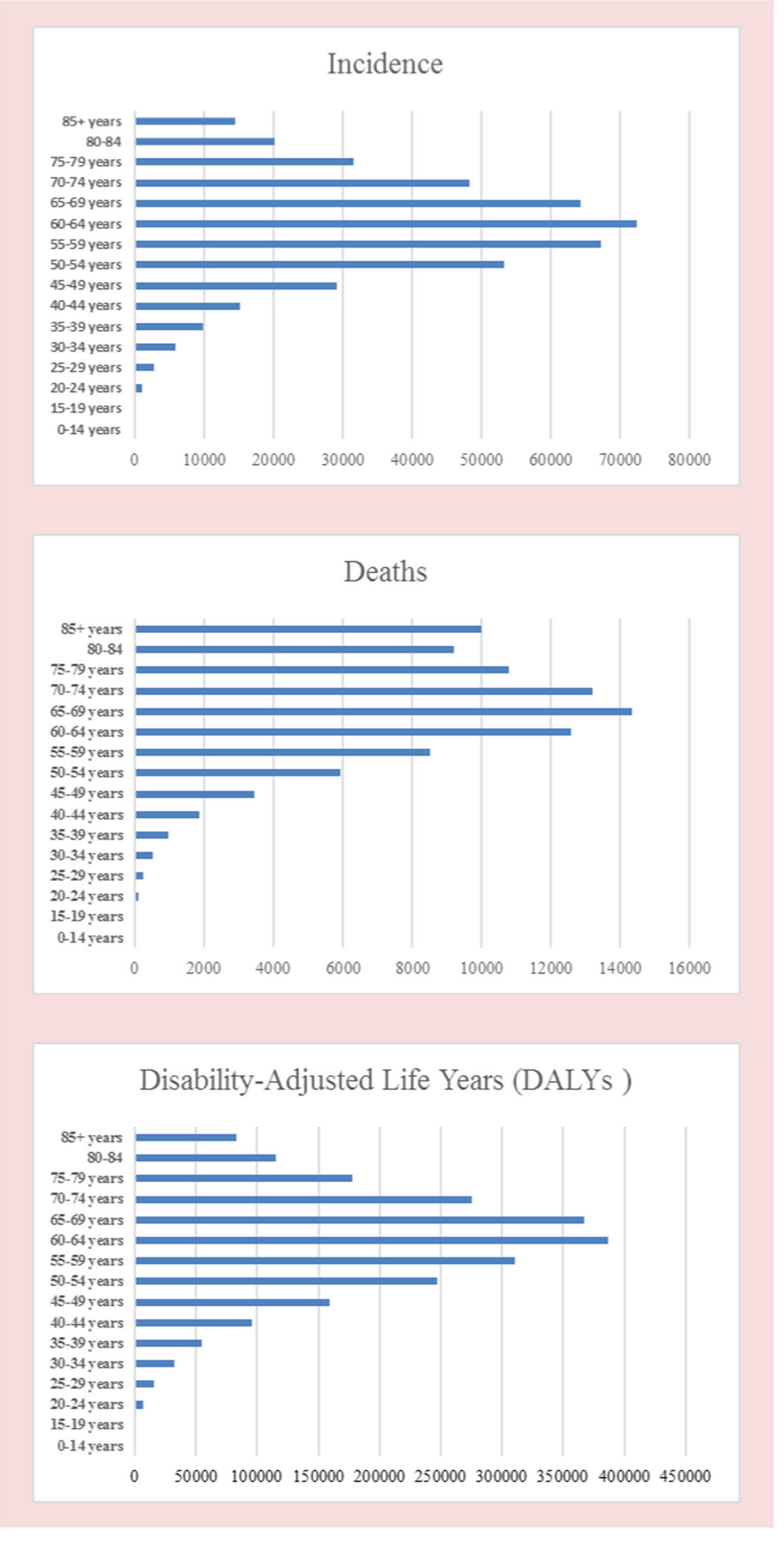

FIGURE 1 Global age-specific incidence, deaths, and disability-adjusted life years cases of uterine cancer in 2019.

TABLE 1 Uterine cancer incidence cases, age-standardized incidence rate, deaths, age-standardized mortality rate, DALYs, age-standardized DALY rates, YLLs, age-standardized YLLs rates, YLDs, and age-standardized YLDs rates in 2019.

	Incidence cases (95% CI)	Incidence ASR per 10^5 (95% CI)	Deathscases (95% CI)	Deaths ASR per 10^5 (95% CI)	DALYsnumber (95% CI)	DALYs ASR per 10^5 (95% CI)	YLLsnumber (95% CI)	YLLs ASR per 10^5 (95% CI)	YLDs number (95% CI)	YLDs ASR per 10^5 (95% CI)
Global	435-,041	9.99	91,641	2.09	2,329,074	53.54	2,109,454	48.49	219,620	5.05
	(397,021–479,729)	(9.12–11.02)	(82,389–101,502)	(1.88–2.32)	(2,092,947–2,560,886)	(48.13–58.84)	(1,901,948–2,319,747)	(43.73–53.28)	(155,374–294,045)	(3.57–6.77)
SDI										
High SDI	168,021	19.16	26,632	2.52	596,794	65.31	510,906	55.40	85,888	9.92
	(148,611–188,553)	(16.94–21.48)	(23,999–28,143)	(2.32–2.64)	(555,850–636,053)	(60.99–69.65)	(476,342–532,669)	(52.32–57.62)	(60,437–114,152)	(6.92–13.28)
High-middle SDI	149,131	13.87	26,426	2.33	667,941	61.50	591,333	54.34	76,608	7.16
	(133,484–165,008)	(12.4–15.37)	(23,965–28,832)	(2.12–2.55)	(606,211–735,232)	(55.81–67.85)	(536,412–647,820)	(49.41–59.54)	(53,709–102,368)	(4.99–9.61)
Low SDI	9530	3.43	5296	2.10	145,258	51.24	141,300	49.87	3957	1.37
	(7770–11,735)	(2.81–4.21)	(4320–6639)	(1.72–2.63)	(117,902–181,516)	(41.73–64.02)	(114,881–175,549)	(40.64–62.32)	(2655–5719)	(0.92–1.96)
Low-middle SDI	29,421	3.94	12,247	1.75	332,222	44.53	318,726	42.76	13,496	1.78
	(25,043–35,620)	(3.36–4.8)	(10,429–15,284)	(1.49–2.21)	(280,870–404,903)	(37.69–54.57)	(268,959–386,040)	(36.18–52.19)	(9248–18,739)	(1.22–2.48)
Middle SDI	78,640	5.70	20,954	1.61	584,639	42.88	545,112	40.04	39,527	2.84
	(64,686–92,030)	(4.72–6.67)	(17,525–24,330)	(1.36–1.87)	(475,787–674,773)	(34.87–49.47)	(442,836–627,041)	(32.65–46.08)	(27,186–56,802)	(1.96–4.07)
World Bank Income Level										
World Bank high income	209,886	19.91	33,461	2.62	742,750	67.47	635,419	57.16	107,332	10.31
	(186,697–234,255)	(17.81–22.17)	(30,197–35,344)	(2.42–2.75)	(690,345–791,137)	(63.04–71.8)	(594,304–664,766)	(54.18–59.53)	(75,678–142,908)	(7.22–13.76)
World Bank low income	7057	3.99	3752	2.34	103,137	57.71	100,141	56.08	2996	1.63
	(5301–8785)	(3–4.92)	(2872–4663)	(1.8–2.89)	(77,908–128,049)	(43.92–71.64)	(75,984–124,644)	(42.68–69.74)	(1930–4332)	(1.06–2.34)
World Bank lower middle income	57,813	4.43	22,335	1.85	613,261	47.08	586,286	45.05	26,975	2.03
	(47,001–66,018)	(3.64–5.07)	(18,344–26,025)	(1.54–2.18)	(491,050–696,110)	(38.11–54.02)	(465,256–674,415)	(36.17–51.7)	(18,233–36,961)	(1.39–2.77)
World Bank upper middle income	159,986	8.84	32,006	1.78	867,697	48.02	785,525	43.48	82,172	4.54
	(139,425–187,583)	(7.71–10.34)	(28,127–37,471)	(1.56–2.08)	(762,477–1,016,761)	(42.13–56.13)	(689,140–915,227)	(38.03–50.62)	(56,868–113,817)	(3.14–6.29)

(Continues)

TABLE 1 (Continued)

	Incidence cases (95% CI)	Incidence ASR per 10^5 (95% CI)	Deathscases (95% CI)	Deaths ASR per 10^5 (95% CI)	DALYsnumber (95% CI)	DALYs ASR per 10^5 (95% CI)	YLLsnumber (95% CI)	YLLs ASR per 10^5 (95% CI)	YLDs number (95% CI)	YLDs ASR per 10^5 (95% CI)
Continents										
Africa	145,398	3.51	5901	1.94	156,862	45.52	151,599	44.05	5263	1.48
	(122,593–173,388)	(2.74–4.18)	(4596–7184)	(1.52–2.33)	(122,009–190,927)	(35.56–55.4)	(118,009–184,856)	(34.37–53.64)	(3477–7443)	(0.98–2.09)
America	115,128	17.10	20,350	2.89	497,028	73.76	438,981	65.10	58047	8.66
	(99,619–133,938)	(14.78–19.88)	(18,918–21,573)	(2.7–3.06)	(465,338–532,013)	(69.08–79)	(414,044–464,208)	(61.48–68.97)	(40,871–78,394)	(6.08–11.72)
Asia	161,731	5.65	36,933	1.48	1,028,897	40.20	955,699	37.37	73,198	2.83
	(144,494–180,469)	(4.76–6.73)	(31,535–44,744)	(1.27-1.8)	(865,607–1,219,021)	(33.73–47.69)	(797,475–1,131,957)	(31.32–44.25)	(49,984–103,311)	(1.94–3.99)
Europe	12,006	21.17	28,253	3.14	641,311	81.10	558,581	70.14	82,730	10.96
	(9330–14,429)	(19–23.64)	(25,733–30,271)	(2.89–3.36)	(589,484–693,644)	(74.46–87.93)	(516,530–599,012)	(64.82–75.52)	(58,432–110,359)	(7.69–14.77)
WHO regions										
African region	8925	3.35	4888	2.03	127,883	47.12	124,136	45.77	3748	1.34
	(7015–10,898)	(2.63–4.04)	(3841–5977)	(1.6–2.46)	(99719–158684)	(36.84–57.98)	(96,963–154,226)	(35.84–56.25)	(2513–5328)	(0.89–1.91)
Eastern Mediterra-nean region	12,873	5.61	4629	2.32	133,805	58.60	127,743	56.06	6063	2.55
	(9590–15,590)	(4.28–6.81)	(3653–5832)	(1.85–2.93)	(101,613–165,991)	(45.64–73.5)	(96,936–158,692)	(43.63–70.43)	(3882–8589)	(1.67–3.63)
European region	166,359	20.74	29,313	3.15	673,137	81.70	588,069	70.98	85,068	10.72
	(149,203–185,437)	(18.62–23.14)	(26,741–31,377)	(2.9–3.37)	(620,510–727,009)	(75.13–88.38)	(545,080–629,420)	(65.78–76.21)	(60,087–113,405)	(7.52–14.44)
Region of the Americas	115,128	17.10	20,350	2.89	497,028	73.76	438,981	65.10	58,047	8.66
	(99,619–133,938)	(14.78–19.88)	(18,918–21,573)	(2.7–3.06)	(465,338–532,013)	(69.08–79)	(414,044–464,208)	(61.48–68.97)	(40,871–78,394)	(6.08–11.72)
South-East Asia region	32,361	3.46	12,987	1.48	351,049	37.64	335,962	36.04	15,087	1.59
	(24,263–38,375)	(2.62–4.12)	(10,091–15,541)	(1.15–1.78)	(263,059–416,042)	(28.52–44.6)	(250,552–398,729)	(27.1-42.94)	(9437–21,256)	(1–2.23)
Western Pacific region	97,931	7.08	19,140	1.34	537,583	38.67	486,714	34.99	50,869	3.68
	(80,987–125,008)	(5.81–8.97)	(15,987–24,514)	(1.12–1.71)	(448,870–677,510)	(32.04–48.31)	(402,234–606,061)	(28.65–43.21)	(33,534–74,093)	(2.43–5.33)
GBD region										

TABLE 1 (Continued)

	Incidence cases (95% CI)	Incidence ASR per 10^5 (95% CI)	Deathscases (95% CI)	Deaths ASR per 10^5 (95% CI)	DALYsnumber (95% CI)	DALYs ASR per 10^5 (95% CI)	YLLsnumber (95% CI)	YLLs ASR per 10^5 (95% CI)	YLDs number (95% CI)	YLDs ASR per 10^5 (95% CI)
East Asia and Pacific —WB	113,081	6.93	24,210	1.47	685,743	42.04	627,522	38.47	58,221	3.57
	(93,297–137,759)	(5.71–8.43)	(20,325–29,391)	(1.23–1.77)	(571,472–806,338)	(34.88–49.09)	(520,048–740,517)	(31.7-45.13)	(38,979–83,151)	(2.38–5.12)
East Asia	70,917	6.55	12,931	1.19	386,025	35.70	348,842	32.27	37,183	3.43
	(55,042–96,591)	(5.07–8.8)	(10,124–17,986)	(0.93–1.65)	(306,607–522,999)	(28.39–47.85)	(270,830–473,492)	(25.06–43.38)	(23,472–55,646)	(2.17–5.15)
Oceania	344	8.58	146	4.18	4565	113.23	4409	109.55	155	3.68
	(191–461)	(4.86–11.31)	(81–195)	(2.44–5.5)	(2486–6176)	(63.01–151.27)	(2407–5982)	(60.82–146.95)	(79–233)	(1.88–5.51)
Southeast Asia	22,135	6.23	7319	2.21	210,937	59.84	200,183	56.85	10,755	2.98
	(14,283–26,648)	(4.1–7.47)	(5132–8654)	(1.6–2.6)	(137,470–251,353)	(39.99–71.06)	(129,203–239,472)	(37.52–67.65)	(6281–15,240)	(1.77–4.23)
Sub-Saharan Africa—WB	8880	3.39	4953	2.09	130,103	48.67	126,401	47.32	3701	1.35
	(7002–10,944)	(2.68–4.11)	(3909–6038)	(1.66–2.53)	(101,876–161,671)	(38.29–60.02)	(99,197–157,677)	(37.28–58.34)	(2484–5267)	(0.91–1.91)
Central Sub-Saharan Africa	923	3.01	549	1.97	15279	48.58	14,900	47.40	379	1.18
	(653–1313)	(2.14–4.32)	(392–783)	(1.42–2.8)	(10,883–21,891)	(34.5–69.88)	(10,631–21,278)	(33.7–67.83)	(231–613)	(0.73–1.91)
Eastern Sub-Saharan Africa	3271	3.70	1918	2.41	51,338	56.64	49,996	55.20	1342	1.44
	(2357–4076)	(2.64–4.57)	(1345–2381)	(1.7–3.01)	(36,529–64,207)	(40.16–70.28)	(35,589–62,177)	(39.09–68.38)	(843–1971)	(0.92–2.1)
Southern Sub-Saharan Africa	1675	5.08	866	2.77	20,787	62.63	20,080	60.54	707	2.09
	(1188–1951)	(3.57–5.87)	(604–998)	(1.92–3.18)	(14,759–24,260)	(44.04–73.04)	(14,282–23,511)	(42.53–70.67)	(446–971)	(1.32–2.86)
Western Sub-Saharan Africa	2677	2.64	1511	1.66	39,565	38.46	38,451	37.41	1114	1.05
	(2147–3598)	(2.13–3.58)	(1225–2050)	(1.36–2.27)	(31,678–53,152)	(31.19–51.7)	(30,797–51,923)	(30.25–50.37)	(726–1661)	(0.69–1.56)
South Asia —WB	23,008	3.01	10,625	1.48	280,650	36.53	270,409	35.21	10,241	1.31
	(18,475–28,217)	(2.43–3.69)	(8469–13,503)	(1.18–1.88)	(222,734–353,409)	(29.02–46.14)	(214,624–342,284)	(27.96–44.72)	(6694–14,749)	(0.86–1.88)
South Asia	21,825	2.94	10,251	1.47	270,456	36.23	260,791	34.95	9665	1.28
	(17,275–26,690)	(2.34–3.61)	(8134–13,078)	(1.16–1.87)	(213,055–341,844)	(28.51–45.91)	(205,193–330,398)	(27.54–44.41)	(6277–13,970)	(0.83–1.84)

(Continues)

TABLE 1 (Continued)

	Incidence cases (95% CI)	Incidence ASR per 10^5 (95% CI)	Deathscases (95% CI)	Deaths ASR per 10^5 (95% CI)	DALYsnumber (95% CI)	DALYs ASR per 10^5 (95% CI)	YLLsnumber (95% CI)	YLLs ASR per 10^5 (95% CI)	YLDs number (95% CI)	YLDs ASR per 10^5 (95% CI)
Latin America and Caribbean—WB	28,924	7.96	9194	2.54	22,7037	62.58	213,105	58.75	13,931	3.83
	(25,680–32,820)	(7.06–9.03)	(8383–10,145)	(2.32–2.8)	(206,450–253,378)	(56.91–69.86)	(194,221–236,180)	(53.54–65.12)	(9960–18,871)	(2.74–5.18)
Andean Latin America	2902	9.75	1019	3.53	25,318	85.55	23,961	81.02	1357	4.53
	(2280–3772)	(7.65–12.67)	(808–1340)	(2.8–4.63)	(19,716–33,212)	(66.72–112.49)	(18,929–31,501)	(63.97–106.37)	(871–2061)	(2.91–6.86)
Caribbean	4837	17.83	1564	5.68	39,693	146.98	37,404	138.52	2289	8.46
	(4105–5678)	(15.11–20.97)	(1342–1819)	(4.86–6.62)	(33,595–46,791)	(124.22–173.54)	(31,533–44,233)	(116.8–164.37)	(1583–3060)	(5.84–11.32)
Central Latin America	8368	6.40	2337	1.84	61,386	47.36	57,233	44.20	4153	3.16
	(7041–9917)	(5.39–7.58)	(1986–2730)	(1.57–2.16)	(52,093–72,130)	(40.25–55.58)	(48,372–67,124)	(37.4–51.72)	(2849–5659)	(2.17–4.31)
Tropical Latin America	9347	6.97	3185	2.40	76,612	57.25	72,153	53.93	4458	3.32
	(8724–10,021)	(6.5–7.48)	(2932–3419)	(2.2–2.57)	(71,458–81,999)	(53.41–61.27)	(67,522–76,987)	(50.44–57.54)	(3157–5946)	(2.35–4.42)
Middle East and North Africa—WB	8834	5.12	2186	1.47	61,703	36.25	57,223	33.71	4480	2.54
	(6469–10,649)	(3.83–6.13)	(1652–2591)	(1.14–1.73)	(45,354–74,453)	(27.11–43.16)	(41,899–68,870)	(25.06–40.31)	(2867–6263)	(1.67–3.52)
North Africa and Middle East	12,514	5.41	3229	1.58	89,656	39.33	83,373	36.67	6283	2.66
	(8467–14,857)	(3.71–6.39)	(2350–3811)	(1.17–1.85)	(62,703–107,519)	(28.15–46.59)	(58,668–99,615)	(26.36–43.49)	(3790–8780)	(1.62–3.7)
Europe and Central Asia—WB	164,951	20.77	29,035	3.15	666,838	81.74	582,483	71.00	84,355	10.74
	(147,923–183,589)	(18.64–23.16)	(26,483–31,071)	(2.9–3.37)	(614,472–719,872)	(75.15–88.5)	(539,766–623,903)	(65.81–76.24)	(59,594–112,477)	(7.54–14.46)
Central Asia	5456	11.72	1350	3.20	41,088	89.73	38,357	83.94	2731	5.78
	(4862–6113)	(10.47–13.11)	(1210–1507)	(2.88–3.57)	(36,618–46,349)	(80.18–100.92)	(34,207–43,118)	(75.09–93.9)	(1912–3668)	(4.03–7.74)
Central Europe	21,860	20.52	4724	3.79	107,516	96.48	96,512	86.00	11,004	10.48
	(18,941–25,296)	(17.68–23.86)	(4102–5429)	(3.28–4.36)	(93,143–123,603)	(83.29–111.56)	(83,494–111,417)	(74.12–99.41)	(7717–14,894)	(7.26–14.21)

TABLE 1 (Continued)

	Incidence cases (95% CI)	Incidence ASR per 10^5 (95% CI)	Deathscases (95% CI)	Deaths ASR per 10^5 (95% CI)	DALYsnumber (95% CI)	DALYs ASR per 10^5 (95% CI)	YLLsnumber (95% CI)	YLLs ASR per 10^5 (95% CI)	YLDs number (95% CI)	YLDs ASR per 10^5 (95% CI)
Eastern Europe	52,513	27.50	8439	3.92	219,203	110.79	192,147	96.52	27,055	14.27
	(44,705–61,827)	(23.25–32.58)	(7309–9673)	(3.39–4.51)	(190,175–252,530)	(95.86–128.31)	(166,072–222,363)	(82.9–112.22)	(18,596–38,058)	(9.75–20.18)
High-income	193,475	19.87	30,302	2.54	669,650	65.75	570,660	55.45	98,991	10.30
	(171,243–216,907)	(17.68–22.3)	(27,197–32,000)	(2.35–2.66)	(623,510–712,015)	(61.64–69.87)	(533,721–594,037)	(52.6–57.41)	(69,238–131,166)	(7.17–13.73)
Australasia	2688	11.26	654	2.40	13804	56.30	12,475	50.64	1329	5.66
	(2178–3320)	(9.13–13.94)	(574–722)	(2.13–2.65)	(12,360–15,232)	(50.79–61.96)	(11,221–13,686)	(45.88–55.41)	(896–1864)	(3.79–8.03)
High-income Asia Pacific	17,999	11.32	3425	1.47	76,746	42.38	67,446	36.40	1756	5.98
	(14,655–21,639)	(9.21–13.68)	(2885–3756)	(1.3–1.58)	(68,873–83,458)	(38.85–45.96)	(60,499–72,177)	(33.6–38.66)	(1134–2500)	(3.9–8.59)
High-income North America	86647	27.82	11,264	3.23	27,2493	85.62	228,157	71.28	44,336	14.34
	(72,240–103,730)	(23.11–33.44)	(10,460–11,838)	(3.03–3.38)	(254,058–291,032)	(79.99–91.48)	(217,322–237,560)	(68.2–73.99)	(30,857–60,511)	(9.91–19.69)
Southern Latin America	3644	8.23	1145	2.40	25,423	56.68	23,667	52.66	42,269	4.02
	(2860–4590)	(6.43–10.38)	(1041–1253)	(2.19–2.62)	(23,123–27,906)	(51.56–62.19)	(21,647–25,747)	(48.17–57.34)	(29,659–56,096)	(2.58–5.75)
Western Europe	82,497	19.62	13,814	2.59	281,184	63.23	238,915	53.02	9300	10.22
	(70,937–94,175)	(16.98–22.47)	(12,221–14,709)	(2.35–2.74)	(256,983–301,833)	(58.28–67.78)	(219,238–251,783)	(49.57–55.63)	(6102–13,300)	(7.08–13.73)

Abbreviations: ASR, age-standardized rates; CI, confidence interval; DALY, disability-adjusted life year; SDI, sociodemographic index; WHO, World Health Organization; YLD, years lived with disability; YLL, years of life lost.

FIGURE 2 Distribution of incidence, death, and disability-adjusted life year cases of uterine cancer based on sociodemographic index and World Bank Income level in 2019.

Among the continents, the highest ASDR was reported in Europe, while the lowest was observed in Asia.

The highest ASDR for UC among WHO regions was found in the European Region (3.15 per 100,000 populations). The lowest was reported in the Western Pacific Region (1.34 per 100,000).

In the GBD regions, the highest ASDR is seen in the Caribbean region (5.68 per 100,000 for each region) and the lowest in East Asia (1.19 per 100,000). More details are presented in Table 1 and Figures 2, 3, and 4.

3.4 | Burden of UC

In 2019, 2,329,074 (95% CI: 2,092,947–2,560,886) DALYs due to UC were reported worldwide, of which 2,109,454 (95% CI: 1,901,948–2,319,747) cases were related to YLLs and 219,620 (95% CI: 155,374–294,045) cases were related to years lived with disability (YLDs). The age-standardized DALYs rate (DALYs ASR) of UC worldwide was 53.54 (95% CI: 48.13–58.84) per 100,000 inhabitants, of which 48.49 (95% CI: 43.73–53.28) cases were related to YLLs and 5.05 (95% CI: 3.57–6.77) cases were related to YLDs.

Worldwide, the highest ASR of DALYs has been reported in American Samoa (285.41), Grenada (283.09), Solomon Islands (221.03), Northern Mariana Islands (207.34), Saint Vincent and the Grenadines (205.68), Micronesia (Federated States of Micronesia) (191.76), Nauru (191.06), Marshall Islands (184.53), and Guyana (184.35), respectively.

The lowest ASR of DALYs has been observed in Palau (14.07), Algeria (16.76), Nigeria (18.04), San Marino (20) Republic of Korea (21.63), Bangladesh (22.15), Oman (22.28), Sudan (25.32), and Yemen (25.74), respectively.

Statistics show that the highest ASR of DALYs for UC occurs in countries with high SDI and the lowest rates occur in countries with middle SDI.

According to the World Bank classification, the ASR of DALYs for UC is highest in the World Bank High-Income category and the lowest in World Bank Lower Middle Income.

FIGURE 3 Distribution of incidence, death, and disability-adjusted life year cases of uterine cancer among continents and WHO regions in 2019.

Among the continents, the highest ASR of DALYs was reported in Europe, while the lowest was observed in Asia worldwide.

The highest ASR of DALYs for UC among WHO regions was found in the European Region. The lowest was reported in the Region of the South-East Asia Region.

In the GBD regions, the highest ASR of DALYs is seen in the Caribbean and the lowest in East Asia. More details are presented in Table 1 and Figures 2, 3, and 4.

3.5 | The correlation between global incidence, mortality, burden of UC and SDI, tobacco, dietary risks, and metabolic risk factors

The ASIR of UC were significantly correlated with SDI ($r = 0.622$, $p < 0.001$), tobacco ($r = 0.445$, $p < 0.001$), smoking ($r = 0.632$, $p < 0.001$), alcohol use ($r = 0.507$, $p < 0.001$), chewing tobacco ($r = -0.283$, $p < 0.001$), diet low in fruits ($r = -0.237$, $p < 0.001$), diet low in vegetables ($r = -0.356$, $p < 0.001$), diet low in whole grains ($r = 0.300$, $p < 0.0001$), diet high in red meat ($r = 0.454$, $p < 0.001$), diet high in processed meat ($r = 0.449$, $p < 0.001$), diet high in trans fatty acids ($r = 0.130$, $p < 0.001$), diet low in calcium ($r = -0.576$, $p < 0.001$), high fasting plasma glucose ($r = 0.169$, $p < 0.001$), high BMI ($r = 0.304$, $p < 0.001$).

The ASDR of UC were significantly correlated with chewing tobacco ($r = -0.180$, $p < = 0.01$), diet low in vegetables ($r = 0.227$, $p < 0.001$), diet low in whole grains ($r = 0.138$, $p = 0.049$), diet high in processed meat ($r = -0.145$, $p = 0.035$), diet high in trans fatty acids ($r = -0.174$, $p = 0.013$), high fasting plasma glucose ($r = 0.449$, $p < 0.001$), high BMI ($r = 0.231$, $p = 0.001$).

The age-standardized **DALYs** rates of UC were significantly correlated with Chewing tobacco ($r = -0.172$, $p = 0.014$), diet low in vegetables ($r = 0.200$, $p = 0.004$), diet low in whole grains ($r = 0.150$, $p = 0.033$), diet high in processed meat ($r = -0.152$, $p = 0.030$), diet high in trans fatty acids ($r = -0.171$, $p = 0.014$), high fasting plasma glucose ($r = 0.469$, $p < 0.001$), high BMI ($r = 0.214$, $p = 0.002$).

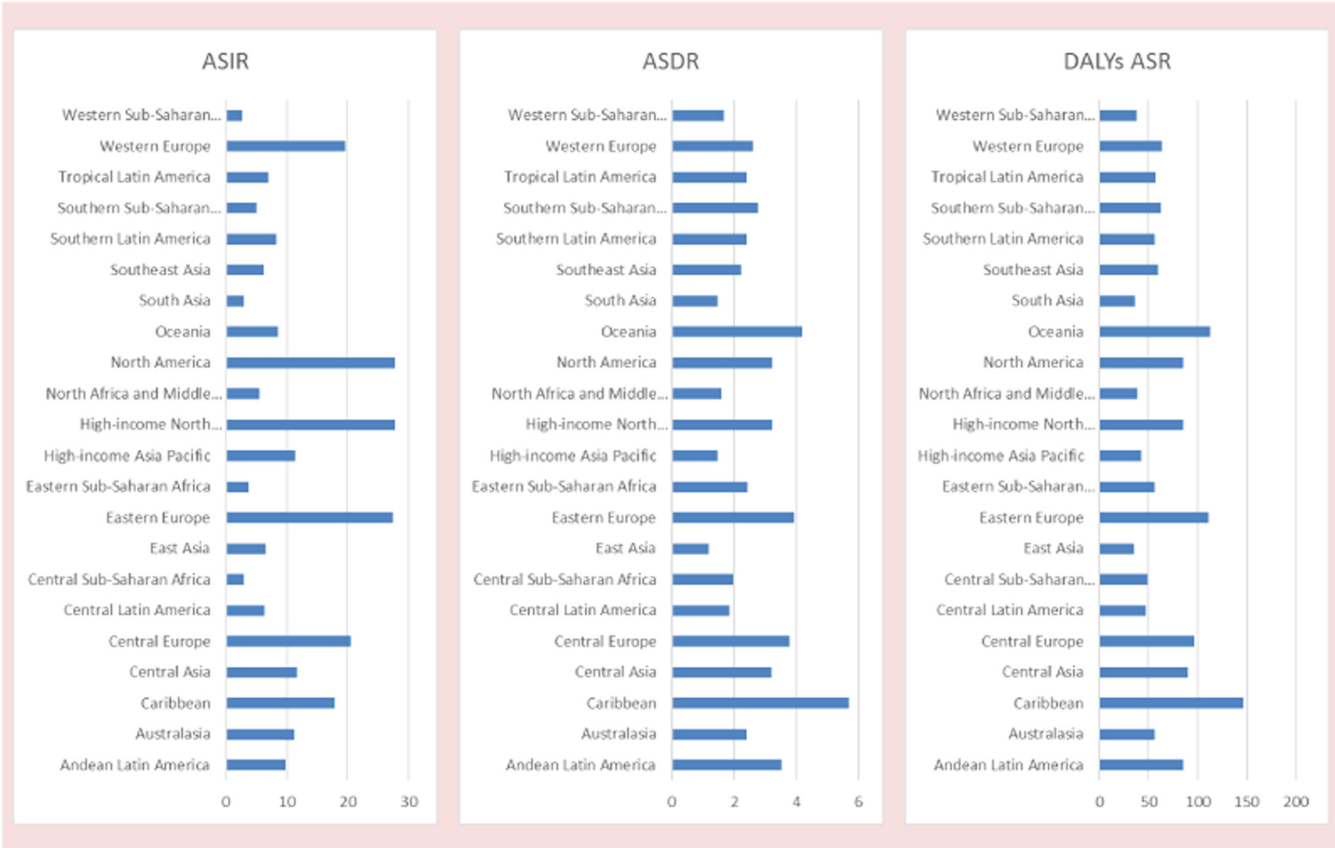

FIGURE 4 The age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), and age-standardized disability-adjusted life years rate (DALYs ASR) of uterine cancer in 22 Global Burden of Disease regions, 2019.

4 | DISCUSSION

According to GBD-2019, the highest incidence, mortality, and DALY of UC are in Europe. Race, ethnicity, economic status, level of education and awareness, co-morbidities, access, grade, and histological type of tumor are the most important causes of inequality in this cancer.[24,25]

Racial differences justify most of these inequalities. This disease has the highest incidence in Europe and the lowest in Africa. Factors such as obesity, metabolic syndrome, hormone therapy, genetic predisposition such as Lynch syndrome and population aging contribute to this statistical difference.[5] Although the incidence of this disease is lower in black women, mortality is higher in them. Lack of awareness, silence about menopause, considering postmenopausal bleeding as normal, and reduced access to and limited resources of health care system cause black women to be diagnosed in advanced stages of this cancer with delay in treatment.[26]

The increase in the prevalence of risk factors has led to an increase in the lifetime risk of EC over time. The most obvious pathophysiological feature of EC is hormone dependence,[27] thus estrogen therapy is one of the risk factors of EC in women. The increased risk of EC is associated with the hormone replacement therapy in postmenopausal women, while the combined use of estrogen and progesterone reduces the risk of EC. Doherty reported an odds ratio of 11 for EC in long-term recipients of postmenopausal hormone therapy.[28] Therefore, it is expected that the rate of cancer will not decrease in areas where the use of hormone therapy after menopause is still high.

There are other risk factors for EC, most of which are related to the effect of estrogen. Obesity contributes to carcinogenesis by changing the hormonal environment. It is also an important risk factor for EC before and after menopause. Obesity is the cause of 40% of EC and more than 70% of people with type I cancer are obese. The increasing and parallel trend of obesity with EC in all ages shows a dose-dependent effect, which increases the chance of cancer with an increase in obesity.[29] Compared to normal women, there is a two to five times increase in EC in obese women, and the survival rate of these women is low.[30] In addition to being associated with obesity, nutritional factors play a role in the occurrence of EC. Consumption of animal fats and sugar is associated with an increased risk of EC, and a diet rich in fruits and vegetables is associated with a decreased risk of this cancer. The Western diet, which is rich in animal fats and carbohydrates, is associated with a 60% increase in the incidence of EC.[31] Case–control studies showed that the risk of EC was significantly elevated by 5% for each 10% kilocalorie of total fat intake and by 17% for each 10% g/1000 kcal of saturated fat intake.[32]

EC mainly occurs in postmenopausal women. Therefore, population aging plays a significant role in the trend of EC.[5] In addition to higher disease progression in this group, less use of surgery and adjuvant treatment hinder optimal treatment and, therefore, lead to unfavorable outcome in these patients.[33] In recent years, the role of fertility changes in increasing the incidence of EC has been the focus of many researchers. Accordingly, early menarche, late menopause, increased number of menstrual cycles and nulliparity increase the risk of EC.[4,6,34] In this regard, results of a study showed that obesity, nulliparity, and early menarche are risk factors for EC in premenopausal women.[6]

SDI is associated with lifestyle, dietary patterns, and disease risk factors. The incidence of EC in high SDI areas is higher than in low SDI areas, and this trend has increased in the last three decades, which can be attributed to the westernization diet and aging of the population in these countries.[35]

Today, lifestyle changes and physical activity,[35] not using hormone therapy after menopause and improving people's awareness about cancer are recommended as the primary prevention methods in the high-risk groups.

This study had some limitations such as limitations in the data from some regions which could affect the results of the present study, and lack or inaccuracy of cancer registry data and cytological results in some low-income countries and inaccuracy in statistical estimates. Also, based on the GBD results, data for different classifications of the participant's calorie intake each day is not available.

5 | CONCLUSION

According to GBD-2019, the highest incidence, mortality, and DALY of EC are in Europe. After examining the evidence, traces of diversity can be seen in the inequalities of UC. Race, ethnicity, economic status, level of education and awareness, co-morbidities, access, grade, and histological type of tumor are the most important causes of inequality in this cancer.

AUTHOR CONTRIBUTIONS

Afrooz Mazidimoradi: Conceptualization; data curation; formal analysis; investigation; methodology; writing—original draft; writing—review and editing. **Zohre Momenimovahed**: Conceptualization; data curation; methodology; project administration; software; writing—original draft; writing—review and editing. **Zohre Khalajinia**: Data curation; project administration; writing—original draft; writing—review and editing. **Leila Allahqoli**: Conceptualization; data curation; investigation; methodology; validation; writing—original draft; writing—review and editing. **Hamid Salehiniya**: Conceptualization; data curation; formal analysis; investigation; project administration; writing—original draft; writing—review and editing. **Ibrahim Alkatout**: Conceptualization; investigation; project administration; supervision; validation; writing—original draft; writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data underlying the results presented are available in the article. Also, data are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

In this study, patient consent was not necessary since we used anonymous electronic data, and the study was approved with the ethical code IR.BUMS.REC.1400.414 at the ethics committee of Birjand University of Medical Sciences.

TRANSPARENCY STATEMENT

The lead author Hamid Salehiniya affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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