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TEMPORAL TRENDS OF COLON AND RECTUM CANCER BETWEEN 2010 AND 2019 IN ASIAN COUNTRIES BY GEOGRAPHICAL REGION AND SDI: A COMPARISON WITH GLOBAL DATA

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ABSTRACT – *Objective:* This study aimed to describe the trends in incidence, mortality, and burden of colon and rectum cancer (CRC) in Asia from 2010 through 2019 comparing them with the other global continental data.

Materials and Methods: We collected CRC data from the 2019 Global Burden of Disease (GBD) study from 2010 to 2019 in 49 countries and territories in Asia. For all locations, annual case data and age-standardized rates (ASRs) were used to investigate the incidence, prevalence, mortality, and disability-adjusted life-years (DALYs) of CRC from 2010 to 2019. The relative difference (%) between years was used to show comparative variations of age-standardized rates for the indicators studied.

Results: In 2019, more than 50% of CRC cases and deaths, prevalence, and DALYs occurred in Asian countries. From 2010 to 2019, incidences, deaths, prevalence cases, and Daly's number increased of CRC increased over 1.46, 1.37, 1.52, and 1.31-fold, in Asia. During this period, the age-standardized incidence rate (ASIR), the age-standardized prevalence rate (ASPR), and the age-standardized DALYs rate (DALYs ASR) of CRC increased by 9%, 15%, and 1%, respectively. The age-standardized death rate (ASDR) had a constant trend. At the same time, these rates increased slowly or had a decreasing trend globally and in America and Europe. In 2019, age-specific incidence, death, prevalence, and DALY cases of CRC cancer were peaking at 65–69, 70-74, 65–69, and 65–69 years, respectively. In 2019, the highest ASIR, ASDR, and ASPR of CRC were observed in High-income Asia Pacific countries and the highest DALYs ASR in Southeast Asia countries. While South Asia countries experienced the highest increasing trend in ASIR and ASDR, ASPR, and DALYs ASR, the High-income Asia Pacific countries experienced the highest decreasing trend from 2010 to 2019. In 2019, among high SDI Asian countries, Taiwan had the highest ASIR and ASPR, and Brunei Darussalam had the highest ASDR and DALY ASR. Among high-middle SDIs, Lebanon has the highest ASIR and ASPR, and Malaysia has the highest ASDR and DALYs ASR; among middle SDIs, China has the highest ASIR and ASPR, and Vietnam has the highest ASDR and DALYs ASR; among low-middle SDIs, Palestine has the highest ASIR, ASDR, ASPR, and DALY ASR of CRC cancer. Among low SDI Asian countries, Pakistan has the highest ASIR and ASPR, and, Afghanistan has the highest ASDR and DALY ASR for CRC cancer. For four indicators, in most countries, the ratio of men is higher than women.

Conclusions: Most of the global burden of CRC occurs in Asian countries, and the increasing trend of incidence, death, prevalence, and burden of this cancer in these countries is faster than in other regions. Therefore, it seems necessary to implement appropriate prevention, diagnosis and treatment strategies in Asian countries to reduce the burden of this disease.

KEYWORDS: Colon and rectum cancer, Asia, Incidence, Prevalence, Death, Burden.

INTRODUCTION

CRC is one of the main causes of morbidity and mortality worldwide[1], the third most common malignant neoplasm after lung and breast cancer and the second main cause of cancer death after lung cancer in the world, with 1,931,590 new cases and 935,173 deaths in 2020[2,3]. By 2035, the total number of deaths has been estimated to increase by 60% for rectal cancer, and 71.5% for colon cancer[4]. In 2020, 10% of the global cancer incidence and 9.4% of cancer deaths were related to CRC. According to the projection of aging, human development, and growth of population, it has been estimatd that in 2040, 3.2 million new CRCs will occur in the world. The increase in new CRC cases is especially related to lifestyle and westernization of dietary patterns[5,6]. Thus, a direct, positive and significant correlation has been reported between the ASIR and ASDR of colorectal cancer and the human development index (HDI)[7].

Aging increases the risk of CRC. This cancer is more prevalent in individuals >50 years old. In women and men, the diagnosis median age is 72 and 68, respectively[8]. Lifestyle, body fatness, and dietary patterns are related to the increase in CRC morbidity[9]. Red and processed meat and alcoholic drinks influence the risk of developing CRC. However, physical activity has a protective factor[9,10]. All things considered, CRC is not consistently prevalent worldwide[11]. There is a wide geographical variation in the worldwide distribution of CRC. In low-income and middle-income countries (LMICs), new CRC cases are increasing, because the prevalence of risk factors including smoking, alcohol, unsafe diets, obesity, non-appropriate physical activity, aging, and growth in CRC screening programs are increased[12,13]. In Asia, CRC is the third most common malignant neoplasm after lung and breast cancer and the fourth main cause of cancer death after lung, liver, and stomach cancer, with 1,009,400 new cases and 506,449 deaths in 2020[3]. In Asia, CRC is the most identified cancer among men in Japan, South Korea, Saudi Arabia, Oman, Yemen, UAE, Bahrain, Qatar, and Kuwait[9].

Due to the increase in the incidence and mortality of CRC, this study has been carried out to describe the trend of incidence, mortality, and the burden of CRC using data from the GBD 2019 from 2010 to 2019.

MATERIALS AND METHODS

Source data

Data on the incidence, mortality, prevalence and burden of CRC for 49 Asian countries, 6 GBD regions, the world and 4 continents were extracted from the GBD 2019 study. GBD provides data online and on the data source Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool) based on the International Classification of Diseases 10 (ICD-10) (code C56.9 for CRC cancer). To obtain the comparative assessment of health loss due to 364 diseases and injuries, in GBD, epidemiological indicators (incidence, death, prevalence, year of life lost (YLL), years lived with disability (YLD), and DALY) by time, location, gender, and age group for 204 countries and territories from 1990 to 2019, were estimated[14-16].

This study has extracted data for various classifications of Asian countries based on a socio-demographic index (SDI), and six GBD regions in Asia from 2010-2019 and compared it with other continental and global data. In particular, we used data for North Africa and the Middle East, as 15 of the 21 GBD countries in North Africa and the Middle East are West Asian. Also, in the countries of Southeast Asia, two counties were African.

GBD has developed an international standard form of QALY, called the Disability-adjusted life year (DALY), and is defined as a lost year of healthy living due to premature death and years with a specified severity and duration of the disability.

“Premature” death is a death at an age when one is not expected to die. The expected age at the death of a person is calculated according to the expected mortality for a certain age in a population

standardized to the population of Japan, which has the longest lifetime at birth in the world. The total number of DALYs under a given condition in a population is equal to the sum of years of life lost (YLLs) and years of disability with known severity and duration (YLDs)[16,17]. The SDI is the geometric average of three indicators including lag-distributed income per capita, average educational attainment of people aged 15 years and older, and the total fertility rate in people aged <25 years[18]. This indicator reflected the levels of social and economic conditions which can affect health outcomes in a given location. Based on SDI, countries and territories were categorized into 5 groups: high SDI (≥0·80), high-middle SDI (≥0·69 and <0·80), middle SDI (≥0·61 and <0·69), low-middle SDI (≥0·45 and <0·61), and low SDI (<0·45)[19,20]. A weighted average of the age-specific rates per 100,000 persons within the corresponding age groups of the WHO standard population is known as ASR. ASR has omitted the differences in the age distribution of the population by applying the rates for each population to a standardized population[21].

Ethical considerations

This study was approved by the Ethics Committee of the Jahrom University of Medical Sciences with IR.JUMS.REC.1401.094 code. Due to the use of online and anonymous data, informed consent was not required.

Statistical analysis

The influence of the different age groups composition within populations was removed by using the age-standardized rates (per 100,000 population) of selected epidemiological indicators. A total of 95% confidence intervals (CI) were reported for all data. Comparative changes in ASRs were shown by the relative changes (%) between years. The relative change is calculated by dividing the value of the absolute difference by the value of the year of origin, which is multiplied by 100[22].

The Male/ Female (M/F) ratio was calculated by dividing the male ASRs by the female ASRs of each epidemiological index. The definitions used in this study are available at https://www.healthdata.org/terms-defined and https://www.healthdata.org/gbd/.

RESULTS

Incidence rate of CRC in Asia

Comparison between global data and continents

In Asia, the number of CRC incidences increased from 767626 (95% CI: 720656_812273) in 2010 to 1123665 (95% CI: 1013541_1242692) in 2019, which is over a 1.46-fold increase. In 2019 approximately 52% (1123665/2166168) of CRC cases happened in Asia countries. During this period, the ASIR of CRC with a 9% change, increased from 21.9 (95% CI: 20.47_23.17) per 100,000 in 2010 to 23.88 (95% CI: 21.54_26.4) per 100,000 in 2019, while in the same time, this rate globally increased by 2%, in America was stable, and in Europe decreased by 1% (Figure 1 and **Table S1**). In Asian men, the number of CRC incidences increased from 459086 (95% CI: 426924_493406) in 2010 to 677545 (95% CI: 591882_779148) in 2019, which is approximately a 1.48-fold increase. In 2019 approximately 60.3% of Asia CRC new cases, occurred in Asian men which included 55% (677545/1239735) of global male CRC incidence cases. During this period, the ASIR of CRC with an 11% change, increased from 27.3 (95% CI: 25.42_29.27) per 100,000 in 2010 to 30.25 (95% CI: 26.61_34.47) per 100,000 in 2019, while in the same time, this rate globally increased by 4%, in America by 2% and in Europe decreased by 2% (**Table S2**). In Asian women, the number of CRC incidences increased from 308540 (95% CI: 283559_330264) in 2010 to 446120 (95% CI: 388182_505587) in 2019, which is over a 1.45-fold increase. In 2019 approximately 39.7% of Asia CRC new cases occurred in Asian women which included 48.2% (446120/926433) of global female CRC incidence cases. During this period, the ASIR of CRC with a 7% change, increased from 17.04 (95% CI: 15.54_18.26) per 100,000 in 2010 to 18.16 (95% CI: 15.73_20.55) per 100,000 in 2019; in the same time, this rate globally was stable by 0%, in Africa increased by 10%, while in Europe decreased by 2%, and in American countries by 1% (**Table S3**).

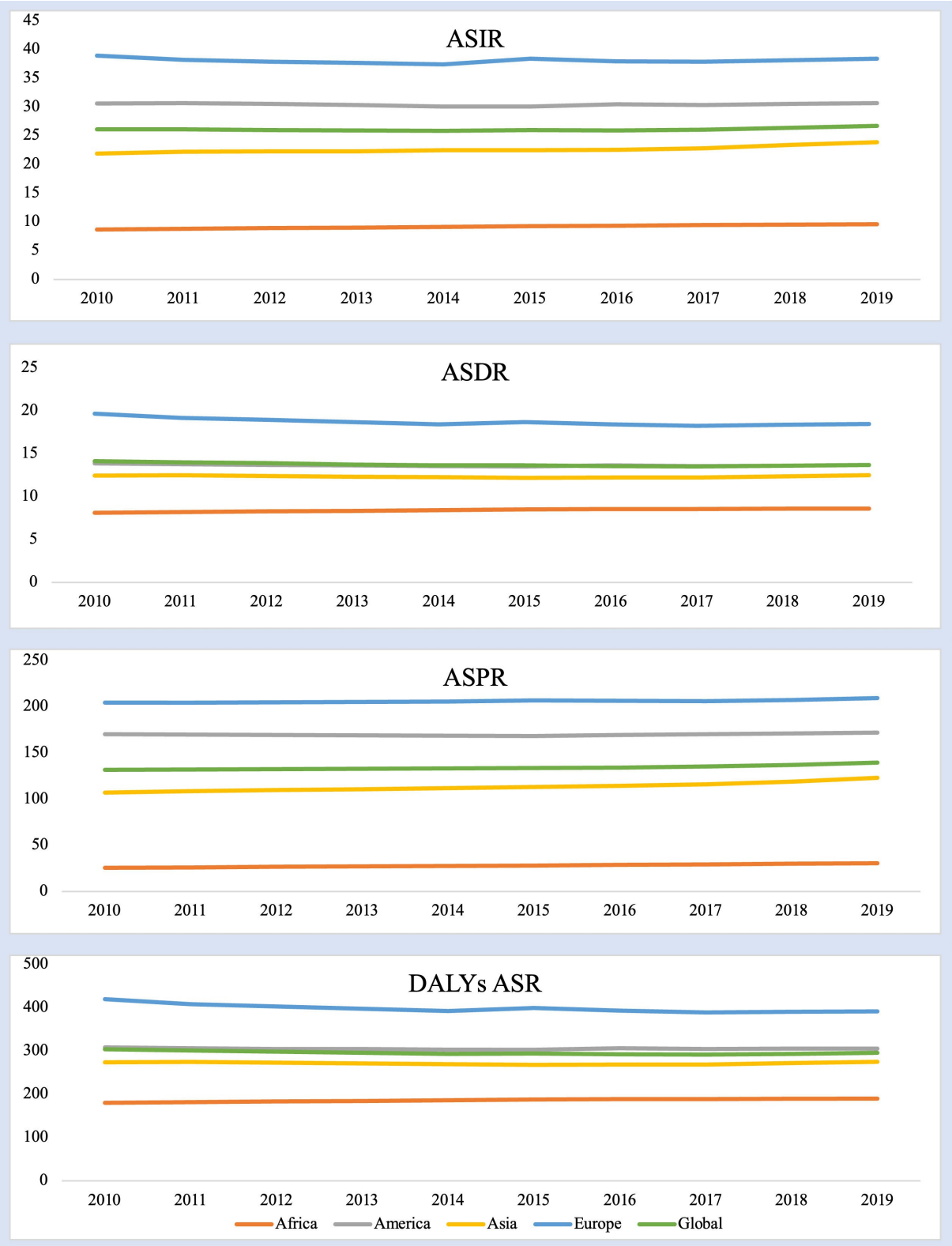

Figure 1. Temporal trend of incidence, prevalence, death and DALYs age standard rates (per 100,000 population) of colon and rectum cancer in ASIA comparison with global data and other continents from 1990 to 2019.

Age distribution

In 2019, age-specific incidence cases of CRC were peaking at 65-69 years generally, 65-69 years in males, and 70-74 in females. In all age groups, the incidence cases of CRC in males was higher, except in ages 85 years and above which in females was higher (Figure 2).

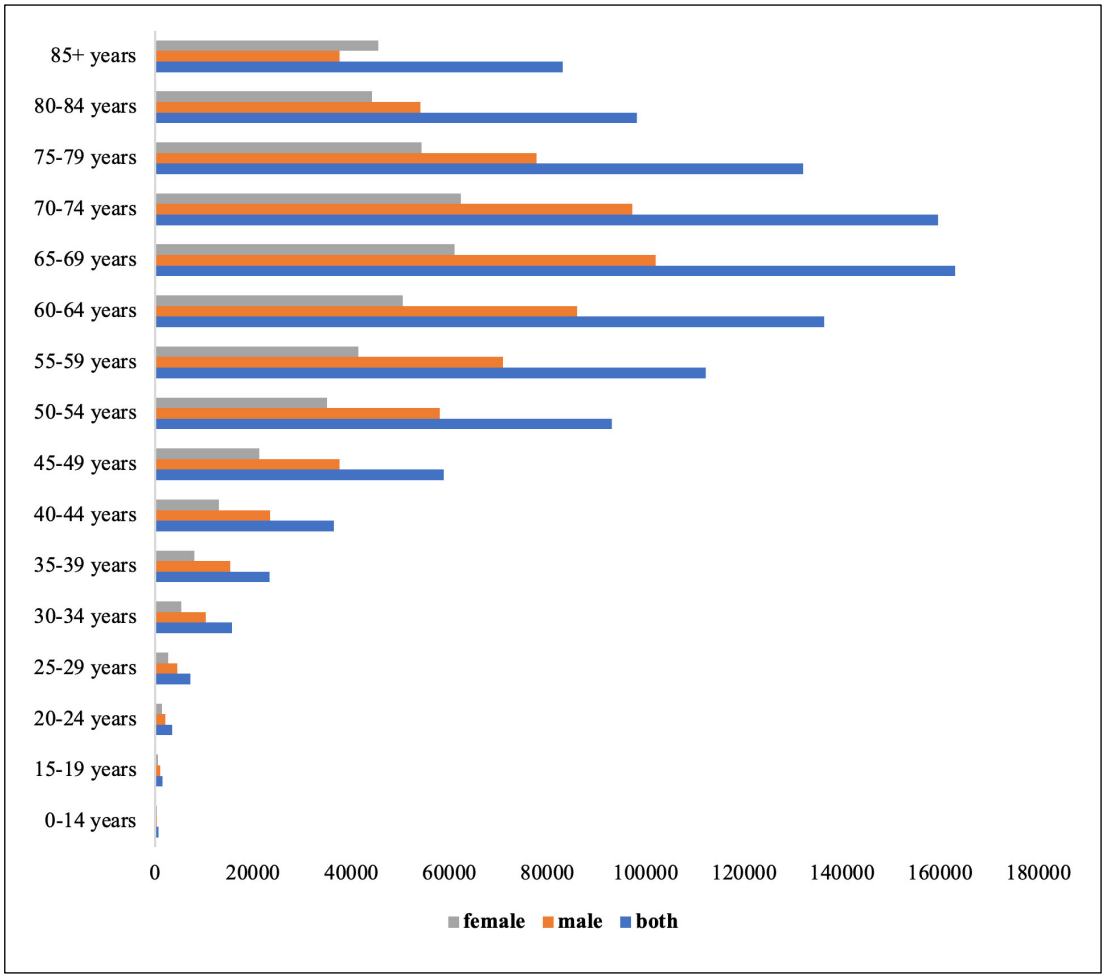

Figure 2. Age specific incidence cases of colon and rectum cancer among sexes in Asia, 2019.

Asian regions

In 2019, the highest ASIR of CRC was observed in High-income Asia Pacific countries (44.58 (95% CI: 38.38_51.09)), with a 4% decrease compared with 2010. While other Asian regions experienced an increasing trend from 7% to 25%. The South Asia countries experienced the highest increasing trend from 2010 to 2019 (by 25%) (Figure 3). In men, the highest ASIR of CRC was observed in High-income Asia Pacific countries (58.74 (95% CI: 49.59_70.03)) with a 5% decrease compared with 2010. While other Asian countries experienced an increasing trend from 9% to 22%. The Southeast Asia region experienced the highest increasing trend from 2010 to 2019 (by 22%). In women, the highest ASIR of CRC was observed in High-income Asia Pacific countries (58.74 (95% CI: 49.59_70.03)); with a 5% decrease compared with 2010. While other Asian regions experienced an increasing trend from 9 to 22%. The Southeast Asia region experienced the highest increasing trend from 2010 to 2019 (by 22%).

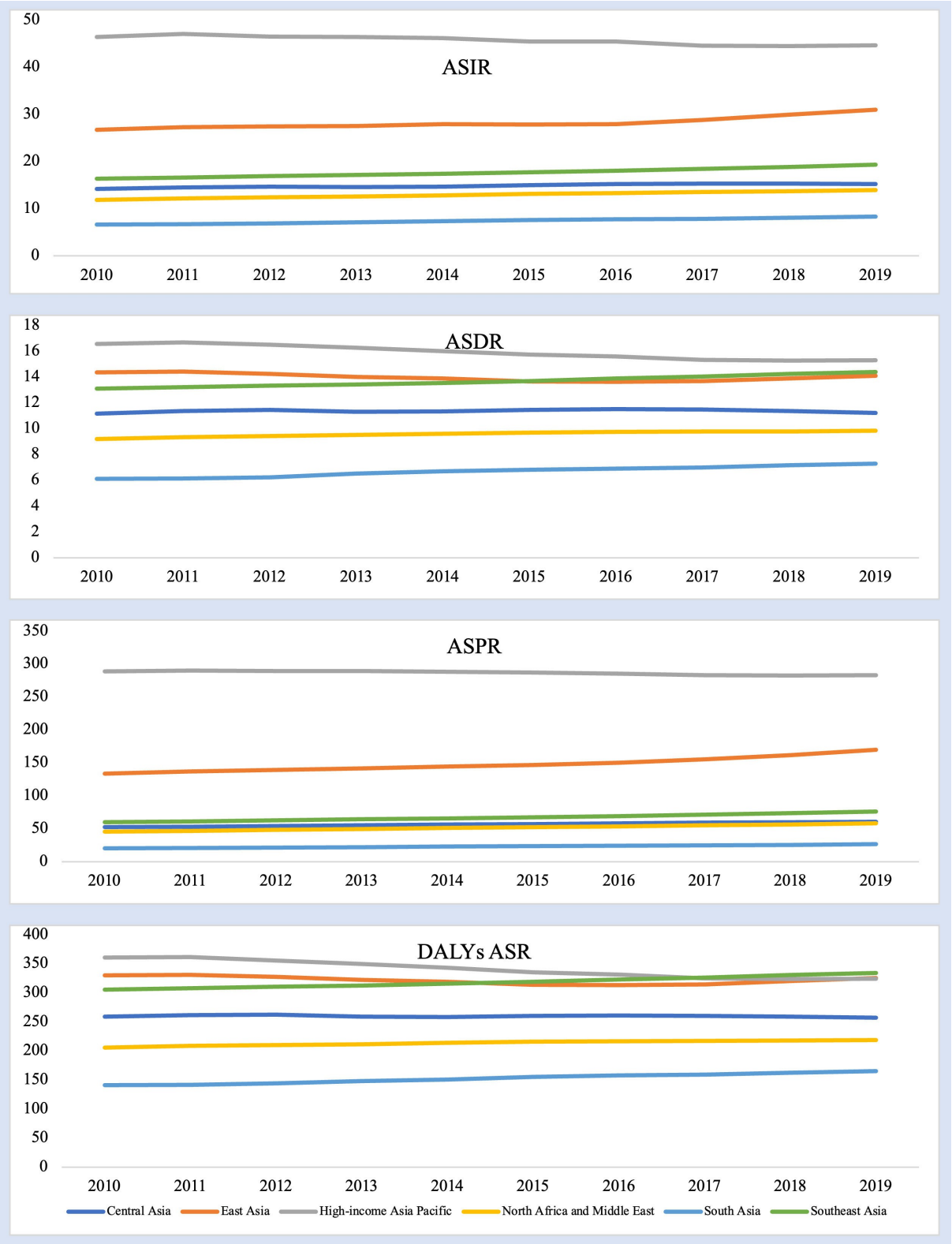

Figure 3. Temporal trend of incidence, prevalence, death and DALYs age standard rates (per 100,000 population) of colon and rectum cancer in Asian regions from 1990 to 2019.

SDI

Among high SDI Asian countries, Taiwan (Province of China) (62.05) and Japan (47.59) have the highest ASIR of CRC, and Saudi Arabia (15.36) has the lowest rate. In this group, 4 countries had an upward trend and 7 countries reported a downward trend from 1990 to 2019. Among high-middle SDI Asian countries, Lebanon (29.83) and Malaysia (29.57) have the highest ASIR of CRC, and Sri Lanka (10.18) has the lowest rate. In this group, only Bahrain and Oman experienced a downward trend, other countries reported an upward trend from 1 (Kazakhstan) to 31% (Sri Lanka) from 1990 to 2019. Among middle SDI Asian countries, China (30.55) and Vietnam (26.36) have the highest ASIR of CRC, and the Syrian Arab Republic (8.54) has the lowest rate. In this group, all countries had an upward trend from 1 (Syrian Arab Republic) to 32% (Turkmenistan) from 1990 to 2019. Among low-middle SDI Asian countries, Palestine (26.12) and Cambodia (16.67) have the highest ASIR of CRC, and Bangladesh (5.63) has the lowest rate. In this group, all countries had an upward trend from 2 (Democratic People's Republic of Korea) to 33% (Palestine) from 1990 to 2019. Among low SDI Asian countries, Pakistan (9.14) has the highest ASIR of CRC, and Nepal (5.88) has the lowest rate. In this group, only Yemen experienced a downward trend, other countries reported an upward trend from 8 (Pakistan) to 30% (Nepal) from 1990 to 2019. More details are presented in **Table S4**.

National comparison

Among Asian countries, 39 countries experienced an increasing trend in the CRC morbidity rate between 2010 and 2019; the greatest increase was detected in Palestine (increase in ASIR = 0.33 (95% CI: 0.11_0.59)) and the greatest decrease was detected in the United Arab Emirates (decrease in ASIR = -0.14 (95% CI: -0.35_0.13)) (Figure 4). In 2019, the highest ASIR (per 100,000) of CRC was reported in Taiwan (Province of China) (62.05), Brunei Darussalam (49.38), Japan (47.59), Singapore (39.93), and Cyprus (38.15). The lowest ASIR of CRC was reported in Bangladesh (5.63), Nepal (5.88), Yemen (7.39), Bhutan (8.03), and the Syrian Arab Republic (8.54). In 2019, the highest ASIR (per 100,000) of CRC in men was reported in Taiwan (Province of China) (80.33), Brunei Darussalam (67.51), Japan (62.44), Republic of Korea (50.47), and Singapore (46.92). The lowest ASIR of CRC was reported in Nepal (5.7), Bangladesh (5.77), Bhutan (7.81), Yemen (7.91), and Afghanistan (8.41). In 2019, the highest ASIR (per 100,000) of CRC in women was reported in Taiwan (Province of China) (45.5), Brunei Darussalam (38.65), Qatar (34.88), Japan (34.61), and Singapore (33.56). The lowest ASIR of CRC was reported in Bangladesh (5.46), Nepal (6.04), Yemen (6.88), the Syrian Arab Republic (7.57), and Pakistan (7.95). Results in detail are presented in **Table S4**.

Male/ female ratio

The ASIR of CRC in India, Nepal, Bhutan, Afghanistan, Maldives, and Qatar is reported to be higher in women than in men. In other countries, the incidence of CRC in men was higher than in women. The highest ratio was reported in Vietnam (2.1 fold) and the lowest ratio was recorded in Qatar (0.6 fold) (Figure 5).

Death rates of CRC in Asia

Comparison between global data and continents

In Asia, the number of CRC deaths increased from 409519 (95% CI: 384501_433756) in 2010 to 560426 (95% CI: 504629_609805) in 2019, which is over a 1.37-fold increase. In 2019, approximately 52% (560426/1085797) of CRC deaths happened in Asia countries. During this period, the ASDR of CRC with an almost constant trend, increased from 12.43 (95% CI: 11.51_13.21) per 100,000 in 2010 to 12.49 (95% CI: 11.25_13.58) per 100,000 in 2019, while in the same time, this rate globally decreased by 3%, in America by 1%, and in Europe by 6% (Figure 1 and **Table S1**). In Asian men, the number of CRC deaths increased from 235991 (95% CI: 220697_251845) in 2010 to 321199 (95% CI: 283355_359519) in 2019, which is over a 1.36-fold increase.

Figure 4. The relative change (%) in age-standardized incidence rate (ASIR), the age-standardized death rate (ASMR), age-standardized DALYs rate (DALYs ASR), and age-standardized prevalence rate (ASPR) of colon and rectum cancer in Asian countries from 1990-2019.

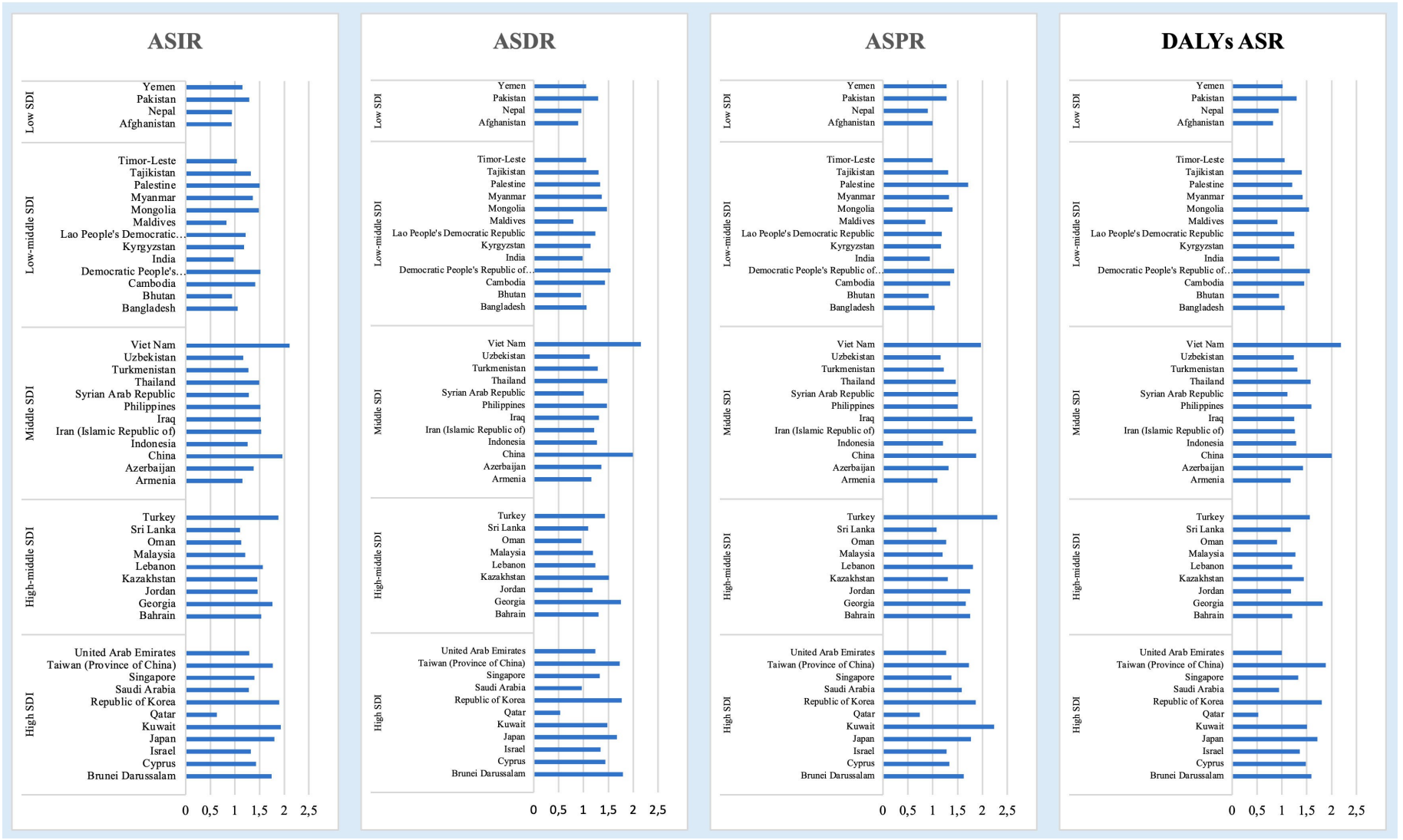

Figure 5. The male/female ratio of age-standardized incidence rate (ASIR), the age-standardized death rate (ASMR), age-standardized DALYs rate (DALYs ASR), and age-standardized prevalence rate (ASPR) of colon and rectum cancer in Asian countries from 1990-2019.

In 2019 more than 57 % of Asia CRC death, occurred in Asian men which included 54.1% (321199/594176) of global male CRC death cases. During this period, the ASDR of CRC with a 1% change, increased from 15.23 (95% CI: 14.2_16.19) per 100,000 in 2010 to15.39 (95% CI: 13.68_17.15) per 100,000 in 2019, while in the same time, this rate globally decreased by 2%, in Europe by 7%, and in America experienced the stable trend with no changes (**Table S2**). In Asian women, the number of CRC deaths increased from 173528 (95% CI: 158429_187197) in 2010 to 239227 (95% CI: 207801_267998) in 2019, which is over a 1.38-fold increase. In 2019 approximately 43% of Asia CRC deaths, occurred in Asian women which included 48.7% (239227/491622) of global female CRC incidence cases. During this period, the ASIR of CRC with 0.3% changes, decreased from 10.02 (95% CI: 9.03_10.83) per 100,000 in 2010 to 9.99 (95% CI: 8.63_11.19) per 100,000 in 2019, while in the same time, this rate globally decreased by 4%, in Europe by 7%, and in American countries by 3% (**Table S3**).

Age distribution

In 2019, age-specific death cases of CRC were peaking at 70–74 years generally, 70-74 years in males, and 85 years and higher in females. In all age groups, death cases of CRC in males were higher than in females, except in ages 85 years and higher which in females was higher (Figure 6).

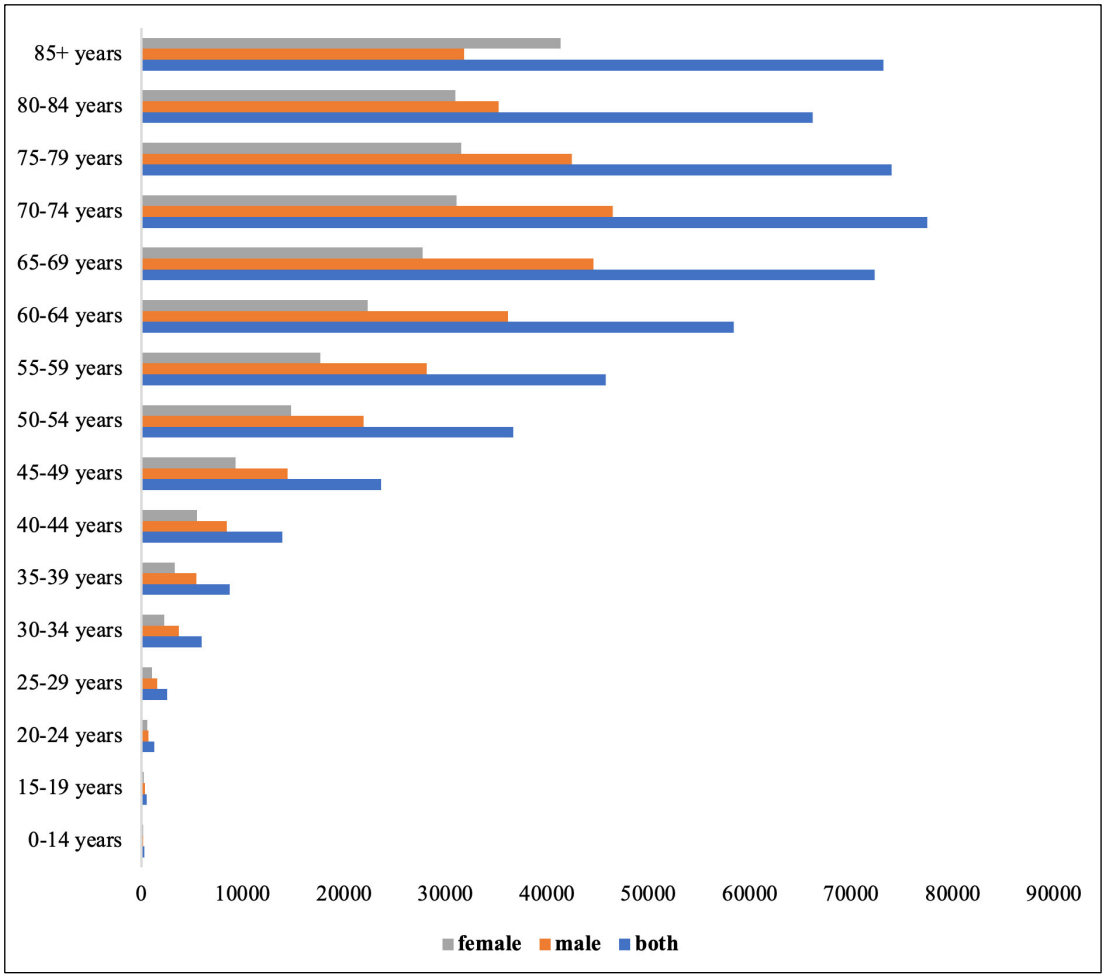

Figure 6. Age specific death cases of colon and rectum cancer among sexes in Asia, 2019.

Asian regions

In 2019, the highest ASDR of CRC was observed in High-income Asia Pacific regions (15.29 (95% CI: 13.42_16.36)) with an 8% decrease compared with 2010. Also in this period, East Asia regions had a decreasing trend of 2%. For Central Asia countries was recorded a stable trend. But other regions experienced an increasing trend from 7 (North Africa and the Middle East) to 19% (South Asia) (Figure 3 and **Table S1**).

In men, the highest ASDR of CRC was observed in Southeast Asia countries (17.4 (95% CI: 14.25_20.32)) with a 14% increase compared with 2010. While High-income Asia Pacific countries experienced a decreasing trend of 10%, other Asian regions experienced an increasing trend of 2 (East Asia) to 14% (South Asia and Southeast Asia) from 2010 to 2019 (**Table S2**). In women, the highest ASDR of CRC was observed in Southeast Asia (11.92 (95% CI: 9.41_14.29)) and High-income Asia Pacific countries (11.71 (95% CI: 9.75_12.82)) in 2019; with a 14% increase compared with 2010. This is while the High-income Asia Pacific region has experienced a downward trend of 6%, and the Southeast Asia region has experienced an upward trend of 6%. Generally, 3 regions recorded an increasing trend of 4 to 25% (South Asia) and 3 regions recorded a decreasing trend of 1 to 6% (**Table S3**).

SDI

In 2019, among high SDI Asian countries, Brunei Darussalam (30.26) and Taiwan (Province of China) (26.26) have the highest ASDR of CRC, and Saudi Arabia (9.66) has the lowest rate. In this classification, between 1990 and 2019, Kuwait experienced a stable trend, and Taiwan (Province of China) recorded an increasing trend; other countries reported an upward trend from 2 (Brunei Darussalam) to 20% (United Arab Emirates). Among high-middle SDI Asian countries, Malaysia (20.32) and Lebanon (17.55) have the highest ASDR of CRC, and Sri Lanka (6.41) has the lowest rate. In this group, 4 countries experienced a downward trend from 2 to 12%, 4 countries reported an upward trend from 3 to 18%, and one had a stable trend from 1990 to 2019. Among middle SDI Asian countries, Vietnam (17.50) and Indonesia (15.58) have the highest ASDR of CRC, and the Syrian Arab Republic (6.28) has the lowest rate. In this group, 3 countries experienced a downward trend from 2 to 4%, 8 countries reported an upward trend from 3 to 15%, and one had a stable trend from 1990 to 2019. Among low-middle SDI Asian countries, Palestine (19.60) and Cambodia (14.02) have the highest ASDR of CRC, and Bangladesh (4.94) has the lowest rate. In this group, only Kyrgyzstan and the Democratic People's Republic of Korea experienced a downward trend, other countries reported an upward trend from 5 (Bangladesh) to 23% (India) from 1990 to 2019. Among low SDI Asian countries, Afghanistan (7.43) has the highest ASDR of CRC, and Nepal (5.40) has the lowest rate. In this group, 2 countries experienced a downward trend, and 2 countries reported an upward trend from 1990 to 2019. More details are presented in **Table S5**.

National comparison

Among Asian countries, 21 countries experienced a decreasing trend in the CRC mortality rate between 2010 and 2019; the greatest increase was detected in Nepal (increase in ASDR = 0.25 (95% CI: 0.01_0.5)) and the greatest decrease was detected in the United Arab Emirates (decrease in ASDR = -0.2 (95% CI: -0.4_0.05)) (Figure 4). In 2019, the highest ASDR (per 100,000) of CRC was reported in Brunei Darussalam (30.26), Taiwan (Province of China) (26.26), Malaysia (20.32), Palestine (19.6), and Lebanon (17.55). The lowest ASDR of CRC was reported in Bangladesh (4.94), Nepal (5.4), Syrian Arab Republic (6.28), Sri Lanka (6.41), and Yemen (6.66).

Among Asian men, the highest ASDR (per 100,000) of CRC was reported in Brunei Darussalam (43.04), Taiwan (Province of China) (33.88), VietNam (25.69), Palestine (23.09), and Malaysia (22.09). The lowest ASDR of CRC was reported in Bangladesh (5.06), Nepal (5.27), Syrian Arab Republic (6.41), Sri Lanka (6.7), and Bhutan (6.79). Among Asian women, the highest ASDR (per 100,000) of CRC was reported in Qatar (25.85), Brunei Darussalam (23.96), Taiwan (Province of China) (19.59), Malaysia (18.54), and Palestine (17.32). The lowest ASDR of CRC was reported in Bangladesh (4.78), Nepal (5.5), Sri Lanka (6.13), Turkmenistan (6.33), and the Syrian Arab Republic (6.38). Results in detail are presented in **Table S5**.

Male/ female ratio

The ASDR of CRC in 8 countries is reported to be higher in women than in men. In other countries, the ASDR of CRC in men was higher than in women. The highest ratio was reported in Vietnam (2.16 fold) and the lowest ratio was recorded in Qatar (0.53 fold). Results in detail are presented in **Table S5** and Figure 5.

Prevalence of CRC in Asia

Comparison between global data and continents

In Asia, the number of cases who lived with CRC increased from 3926365 (95% CI: 3705845_4151031) in 2010 to 5951850 (95% CI: 5376730_6610104) in 2019, which is a 1.52-fold increase. In 2019, approximately 52% (5951850/ 11457627) of CRC prevalence happened in Asian countries. During this period, the ASPR of CRC with a 15% change increased from 107.09 (95% CI: 101.01_113.15) per 100,000 in 2010 to 122.75 (95% CI: 110.97_135.87) per 100,000 in 2019, while in the same time, this rate globally increased by 6%, in America by 1%, and in Europe by 2% (Figure 1 and **Table S1**). In Asian men, the number of CRC prevalence increased from 2368775 (95% CI: 2206991_2549809) in 2010 to 3637709 (95% CI: 3163067_4195548) in 2019, which is over a 1.54-fold increase. In 2019, approximately 61% of patients who lived with CRC in Asia were men which included 55% (3637709/6622600) of global male CRC prevalence cases. During this period, the ASPR of CRC with a 17% change increased from 132.59 (95% CI: 124.04_142.2) per 100,000 in 2010 to 155.3 (95% CI: 135.91_178.27) per 100,000 in 2019; in the same time, this rate globally increased by 8%, in America and Europe by 2% (**Table S2**). In Asian women, the number of CRC prevalence increased from 1557590 (95% CI: 1444551_1660666) in 2010 to 2314141 (95% CI: 2028531_2628039) in 2019, which is approximately a 1.49-fold increase. In 2019, approximately 39% of patients who lived with CRC in Asia were women, which included 48% (2314141/4835027) of global female CRC prevalence cases. During this period, the age-standardized prevalence rate (ASPR) of CRC with an 11% change, increased from 83.19 (95% CI: 76.84_88.65) per 100,000 in 2010 to 92.55 (95% CI: 81.16_105.18) per 100,000 in 2019; in the same time, this rate globally increased by 3%, in Africa by 17%, and in Europe by 2%; while American countries experienced stable trend (**Table S3**).

Age distribution

In 2019, age-specific prevalence cases of CRC were peaking at 65–69 years generally, in males, and females. In all age groups, the prevalence cases of CRC in males was higher than in females, except in ages 85 years and higher which in females was higher (Figure 7).

Asian regions

In 2019, the highest ASPR of CRC was observed in High-income Asia Pacific countries (283.28 (95% CI: 247.9_323.96)) with a 2% decrease compared with 2010. Other Asian regions experienced an increasing trend of 16 (Central Asia) and 32% (South Asia) (Figure 3). In men, the highest ASPR of CRC was observed in High-income Asia Pacific countries (369.83 (95% CI: 314.33_435.54)); with a 3% decrease compared with 2010. In contrast, other regions experienced an increasing trend of 18 (Central Asia) to 33% (North Africa and the Middle East) (**Table S2**). In women, the highest ASPR of CRC was observed in High-income Asia Pacific countries (206.84 (95% CI: 173.65_241.25)) with a 2% decrease compared with 2010. Other countries experienced an increasing trend from 2010 to 2019 from 14 (Central Asia) to 38% (South Asia) (**Table S3**).

SDI

Among high SDI Asian countries, Taiwan (Province of China) (354.70) and Japan (306.54) have the highest ASPR of CRC, and Saudi Arabia (71.06) has the lowest rate. In this group, 6 countries experienced a downward trend from 1 to 4%, and 8 countries reported an upward trend from 1 to 31% from 1990 to 2019. Among high-middle SDI Asian countries, Lebanon (140.75) and Malaysia (122.63) had the highest ASPR of CRC, and Oman (67.01) had the lowest rate. In this group, only Oman experienced a downward trend, other countries reported an upward trend from 6 to 43%, and one had a stable trend from 1990 to 2019. Among middle SDI Asian countries, China (167.67) and Vietnam (113.64) have the highest ASPR of CRC, and Turkmenistan (35.04) have the lowest rate. In this group, all countries experienced an upward trend of 6 to 41% from 1990 to 2019. Among low-middle SDI Asian countries, Palestine (101.69) and the Democratic People's Republic of Korea (65.03) have the highest ASPR of CRC, and Bangladesh (17.96) has the lowest rate. In this group, all countries experienced an upward trend of 7 to 47% from

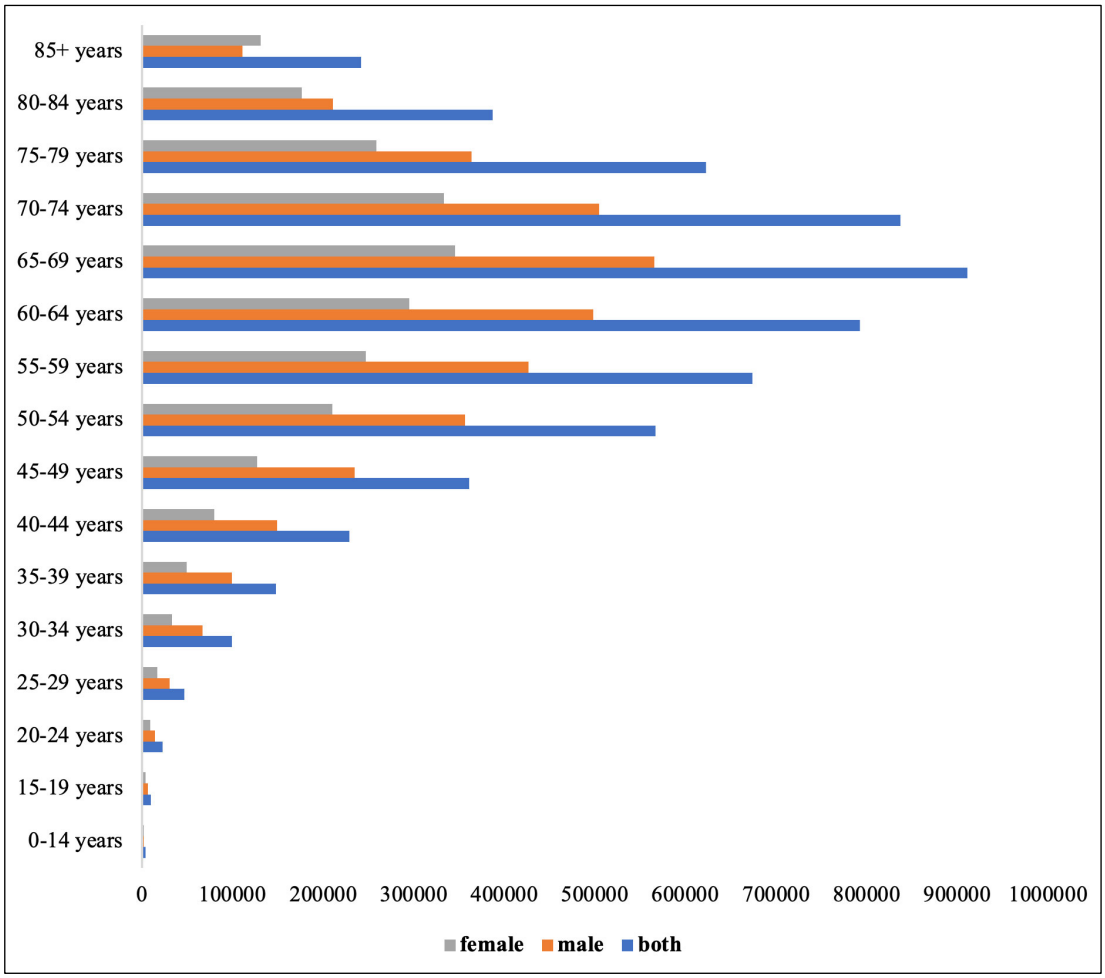

Figure 7. Age specific prevalence cases of colon and rectum cancer among sexes in Asia, 2019.

1990 to 2019. Among low SDI Asian countries, Pakistan (28.03) has the highest ASPR of CRC, and Nepal (17.10) has the lowest rate. In this group, all countries experienced an upward trend of 3 to 37% from 1990 to 2019. More details are presented in **Table S6**.

National comparison

Among Asian countries, only 7 countries experienced a decreasing trend in the CRC prevalence rate between 2010 and 2019; the greatest increase was detected in Palestine (increase in ASPR = 0.47 (95% CI: 0.21_0.76)) and the greatest decrease was detected in Oman (decrease in ASPR = -0.06 (95% CI: -0.23_0.23)) (Figure 4).

In 2019, the highest ASPR (per 100,000) of CRC was reported in Taiwan (Province of China) (354.7), Japan (306.54), Singapore (246.74), Brunei Darussalam (229.89), and Cyprus (227). The lowest ASPR of CRC was reported in Nepal (17.1), Bangladesh (17.96), Yemen (23.39), Afghanistan (24.15), and Bhutan (25.68).

In Asian men, the highest ASPR (per 100,000) of CRC was reported National distribution of CRC among men in Taiwan (Province of China) (454.35), Japan (398.4), Republic of Korea (299.76), Brunei Darussalam (297.65), and Singapore (287). The lowest ASPR (per 100,000) of CRC was reported in Nepal (16.12), Bangladesh (18.25), Afghanistan (24.23), Bhutan (24.63), and Yemen (26.27).

In women, the highest ASPR (per 100,000) of CRC was reported in Taiwan (Province of China) (262.75), Japan (224.79), Singapore (209.14), Cyprus (195.56), and Brunei Darussalam (182.89). The lowest ASPR (per 100,000) of CRC was reported in Bangladesh (17.56), Nepal (17.94), Yemen (20.58), Afghanistan (24.37), and Pakistan (24.51). Results in detail are presented in **Table S6**.

Male/ female ratio

The ASPR of CRC in 5 countries is reported to be higher in women than in men, and in 2 countries almost equal. In other countries, the prevalence of CRC in men was higher than in women. The highest ratio was reported in Turkey (2.3 fold) and the lowest ratio was recorded in Qatar (0.74 fold) (Figure 5).

Burden of CRC in Asia

Comparison with global data and continents

In Asia, the number of CRC DALYs increased from 10215298 (95% CI: 9657694_10803282) in 2010 to 13366568 (95% CI: 12116850_14566748) in 2019, which is a 1.31-fold increase. In 2019 more than 55% (13366568/24284087) of CRC DALYs happened in Asian countries. During this period, the DALYs ASR of CRC with a 1% change, increased from 273.97 (95% CI: 258.5_289.88) per 100,000 in 2010 to 275.48 (95% CI: 249.63_299.4) per 100,000 in 2019, in the same period, this rate globally decreased by 3%, in America by 1%, and in Europe by 7% (Figure 1 and **Table S1**).

In Asian men, the number of CRC DALYs increased from 6111214 (95% CI: 5737750_6536459) in 2010 to 7970545 (95% CI: 7027387_8969737) in 2019, which is over a 1.30-fold increase. In 2019 approximately 59.6% of CRC DALYs in Asia, occurred in men which included 57.1% (7970545 /13959591) of global male CRC DALYs cases. During this period, the DALYs ASR of CRC with a 1% change, increased from 336.14 (95% CI: 315.91_358.91) per 100,000 in 2010 to 339.52 (95% CI: 300.58_380.96) per 100,000 in 2019, in the same period, this rate globally decreased by 2%, in Europe by 7%; in America had stable trend, and Africa increased by 6% (**Table S2**). In Asian women, the number of CRC DALYs increased from 4104083 (95% CI: 3804060_4407829) in 2010 to 5396023 (95% CI: 4757225_6051611) in 2019, which is approximately a 1.32-fold increase. In 2019 approximately 40.4% of DALYs related to CRC in Asia were women, which included 52.3% (5396023/10324496) of global female CRC DALYs cases. During this period, the DALYs ASR of CRC with an approximately stable trend (0% change), partially increased from 215.9 (95% CI: 199.45_231.77) per 100,000 in 2010 to 216.14 (95% CI: 190.7_242.12) per 100,000 in 2019, while in the same time, this rate globally decreased by 3%, in American countries by 2%, in European countries by 7% (**Table S3**).

Age distribution

In 2019, DALYs cases of CRC were peaking at 65–69 years generally, in males, and females. In all age groups, DALY cases of CRC in males were higher than in females, except in ages 85 years and higher which in females was higher (Figure 8).

Within Asian regions

In 2019, the highest DALYs ASR of CRC was observed in Southeast Asia countries (333.97 (95% CI: 276.63_386.37)) with a 9% increase compared with 2010. Generally, 3 regions recorded an increasing trend of 6 (North Africa and Middle East) to 17% (South Asia); and 3 regions recorded a decreasing trend of 1 (Central Asia and East Asia) to 10% (High-income Asia Pacific) (Figure 3 and **Table S1**).

In men, the highest DALYs ASR of CRC was observed in East Asia countries (440.03 (95% CI: 361.53_533.69) with a 2% increase compared with 2010. Only, High-income Asia Pacific countries experienced a downward trend of 12%. Other Asian regions experienced an increasing trend from 2010 to 2019 from 1(Central Asia) to 13% (Southeast Asia) (**Table S2**).

In women, the highest DALYs ASR of CRC was observed in Southeast Asia countries (269.93 (95% CI: 209.87_327.35)) with a 5% increase compared with 2010. Generally, 3 regions recorded an increasing trend of 3 (North Africa and Middle East) to 23% (South Asia); and 3 regions recorded a decreasing trend of 3 (Central Asia) to 9% (High-income Asia Pacific) (**Table S3**).

SDI

In 2019, among high SDI Asian countries, Brunei Darussalam (626.13) and Taiwan (Province of China) (588.36) have the highest DALYs ASR of CRC, and Kuwait (202.28) has the lowest rate. In this group, 9 countries experienced a downward trend from 1 to 19%, and 2 countries reported an upward trend from 1 to 4% from 1990 to 2019. Among high-middle SDI Asian countries, Malaysia (421.97) and Leba-

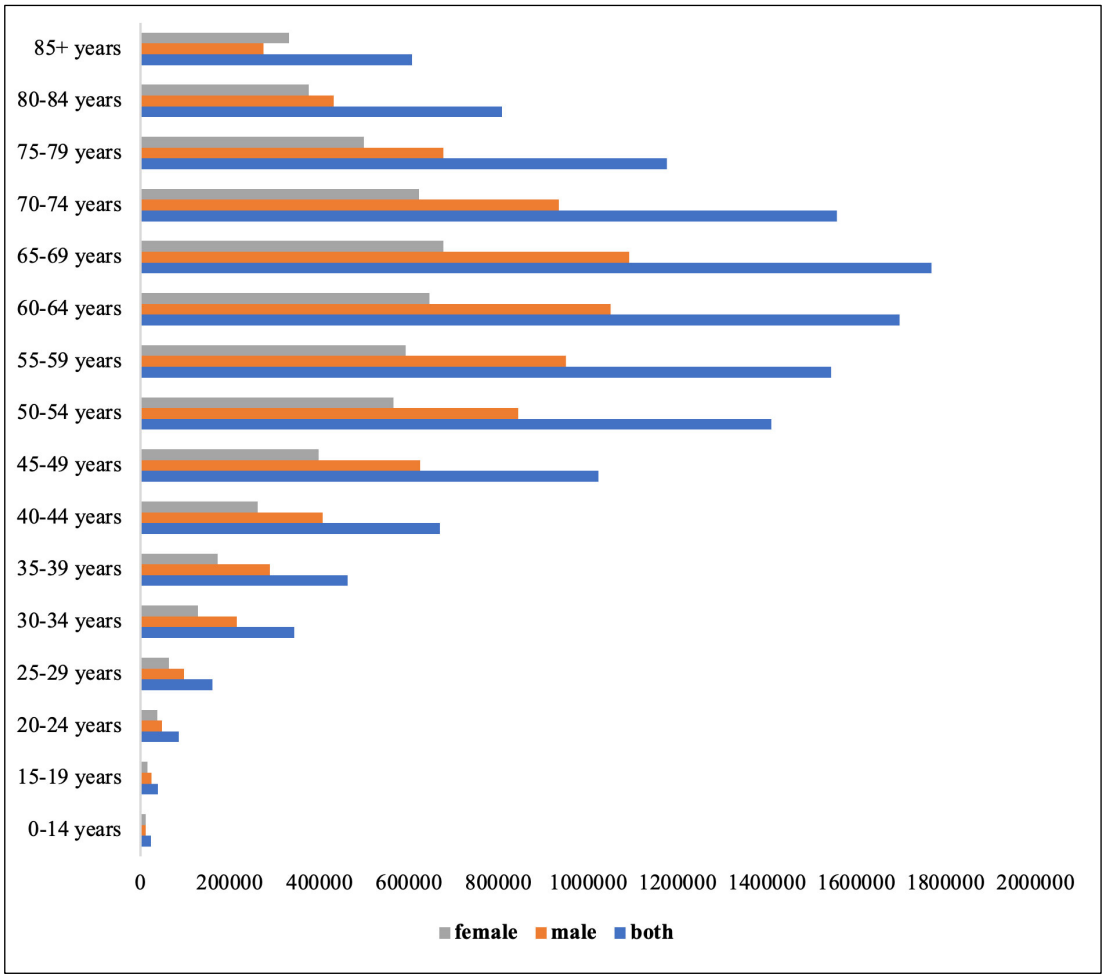

Figure 8. Age specific DALYs cases of colon and rectum cancer among sexes in Asia, 2019.

non (372.53) have the highest DALYs ASR of CRC, and Sri Lanka (137.96) has the lowest rate. In this group, 4 countries experienced a downward trend from 3 to 20%, and 5 countries reported an upward trend from 2 to 21% from 1990 to 2019. In middle SDI Asian countries, Vietnam (409.28) and the Philippines (370.31) have the highest DALYs ASR of CRC, and the Syrian Arab Republic (140.02) has the lowest rate. In this group, 4 countries experienced a downward trend from 1 to 4%, and 8 countries reported an upward trend from 1 to 24% from 1990 to 2019.

Among low-middle SDI Asian countries, Palestine (434.66) and Cambodia (329.14) have the highest ASPR of CRC, and Bangladesh (107.39) has the lowest rate. In this group, 2 countries experienced a downward trend from 1 to 5%, and 11 countries reported an upward trend from 4 to 29% from 1990 to 2019.

Among low SDI Asian countries, Afghanistan (209.28) has the highest DALY ASR of CRC, and Nepal (115.83) has the lowest rate. In this group, Yemen reported a decreasing trend of 3%, and other countries experienced an upward trend of 3 to 23% from 1990 to 2019. More details are presented in **Table S7**.

National comparison

Among Asian countries, 20 countries experienced a decreasing trend in the CRC DALYs ASR between 2010 and 2019; the greatest increase was detected in Turkmenistan (increase in DALYs ASR = 0.24 (95% CI: 0.01_0.54)) and the greatest decrease was detected in Oman (decrease in DALYs ASR = -0.20 (95% CI: -0.35_0.01)) (Figure 4). In 2019, the highest DALYs ASR (per 100,000) of CRC was reported in Brunei Darussalam (626.13), Taiwan (Province of China) (588.36), Palestine (434.66), Malaysia (421.97), and Vietnam (409.28). The lowest DALY ASR of CRC was reported in Bangladesh (107.39), Nepal (115.83), Sri Lanka (137.06), Syrian Arab Repub-

lic (140.02), and Bhutan (145.09). In Asian men, the highest DALYs ASR (per 100,000) of CRC was reported in Brunei Darussalam (808.9), Taiwan (Province of China) (779.54), Viet Nam (589.3), Palestine (481.84), and Malaysia (472.72). The lowest DALYs ASR (per 100,000) of CRC was reported in Bangladesh (109.88), Nepal (111.55), Bhutan (141.23), Syrian Arab Republic (148.31), and Sri Lanka (148.68).

In women, the highest DALYs ASR (per 100,000) of CRC was reported in Brunei Darussalam (508.3), Qatar (445.69), Taiwan (Province of China) (414.4), Palestine (399.28), and Malaysia (370.84). The lowest DALYs ASR (per 100,000) of CRC was reported in Bangladesh (104.22), Nepal (119.32), Sri Lanka (126.67), Syrian Arab Republic (133.42), and Turkmenistan (145.75). Results in detail are presented in **Table S7**.

Male/ female ratio

The DALYs ASR of CRC in 8 countries is reported to be higher in women than in men, and in one almost is equal. In other countries, the DALYs ASR of CRC in men was higher than in women. The highest ratio was reported in Vietnam (2.2 fold) and the lowest ratio was recorded in Qatar (0.52 fold) (Figure 5).

DISCUSSION

The present study was conducted to investigate the CRC trend in Asian countries and compare it with global data from 2010 to 2019. The results showed that in this period, the number of CRC cases and deaths increased by 1.46 and 1.37 times, respectively. Moreover, the number of live CRC cases and CRC DALY also increased by 1.52 and 1.31 times, respectively. According to the results of this study, ASIR increased, ASDR remained almost constant, ASPR increased and the age-standardized DALY rate of CRC increased from 2010 to 2019.

In 2019, 52% of CRC cases were reported in Asia. From 2010 to 2019, the ASIR of CRC increased by 9%. In this period, the number of CRCs has increased in men and women, but a greater increase was reported in men than in women. ASIR increased by 1.48 times in men and by 1.45 times in women. Also, the ASIR of CRC has increased by 11% in men and 7% in women. The highest number of CRC was reported in men aged 65-69 and in women aged 70-74. During this period, ASIR increased in the world, remained stable in America and decreased in Europe. The results of a large-scale meta-analysis that included 8091 CRC cases in 16 studies showed that CRC risk factors include inflammatory bowel disease, history of CRC in first-degree relatives, BMI, cigarette smoking, and red meat consumption. On the other hand, physical activity, fruits and vegetables have a protective role against CRC. It was also revealed that the average risk of CRC in people with a positive family history of CRC compared to people without a family history of CRC is almost twice as high[23]. Concerning BMI, it was shown that the risk of CRC increases by 10% for every 8 kg/m^2 increase in BMI[23]. Another study revealed that increased BMI and waist circumference were associated with an increased risk of colon cancer in both men and women with the relative risk being higher in men. Furthermore, BMI was notably related to rectal cancer in men; however, no relationship between BMI and rectal cancer was reported in women[24]. In a systematic review and meta-analysis, it was shown that a positive history of CRC in first-degree relatives, hyperlipidemia, obesity, and alcohol consumption are risk factors for early-onset CRC[25]. Similarly, a retrospective study in the US about risk factors associated with early-onset CRC showed that individuals aged 18-49 years with a positive family history of CRC were at a higher risk of developing CRC compared to those without a family history[26]. In Asia, non-modifiable risk factors include genetics, ethnicity, age, gender, positive family history and body height. Environmental factors that contribute to CRC are smoking, alcohol consumption, weight, western pattern diet, physical inactivity, chronic diseases and microbiota[27]. CRC and aspects related to gut microbiota have been extensively studied in recent years[28,29]. Kaźmierczak-Siedlecka et al[30] reported an abnormal proportion of short-chain fatty acids known as SCFAs has been observed in all CRC patients. There are multiple beneficial properties associated with microbial-derived metabolites called short-chain fatty acids (SCFAs). Age, diet (primarily fiber intake), and overall health condition are all factors that affect the amount of SCFAs[30]. The abundance, properties, and activity of gut microbes can determine whether or not carcinogenesis is promoted or prevented[31]. It has been demonstrated that the gut microbiota of patients with CRC is altered[32]. To develop gut microbiota as a screening tool for colorectal cancer, it is essential to identify pathogens associated with CRC[33].

The results of this study showed that from 2010 to 2019, the ASDR of CRC in the investigated countries has been almost constant, while during this period, the ASDR of CRC has decreased in America, as well as worldwide, but increased in Europe. In 2019, 52% of CRC deaths occurred in Asian countries.

During this period, ASDR of CRC has increased in men but decreased in women. In 2019, the ASDR of CRC was higher in men than in women. The most cases of death in the entire population were in the age group of 70-74 years, in men 70-74 years, and in women 85 years and older. In 2019, the ASDR of CRC was 12.49 in Asian men and 9.99 in Asian women. It has been shown that in 2018, the age-standardized (world) mortality rate per 100,000 of CRC in men and women was 8.9[34], which is lower than the SRDR of Asian men and women in our study. Overall, mortality is a function of incidence and survival. Therefore, it can increase if the incidence rate overcomes the improvement in survival[35]. However, the most effective way to prevent CRC and reduce CRC mortality in the entire population is to screen average-risk individuals[36]. Population-based screening helps to identify latent disease in average-risk individuals and, therefore, reduce the threat to individuals and/or communities by enabling early-stage interventions[37]. Lifestyle and health service variables were shown to have an impact on cancer deaths[38]. So, cancer death may be reduced with the help of a healthy lifestyle and improved health services. CRC progress takes years and most polyps never become cancerous but in general, a course of 10 to 15 years is required for a polyp to form a malignant tumor. So, regular screening, detecting, and removing polyps at the early stage is crucial in CRC prevention. Current diagnosis can detect only 40% of CRC cases in the early stages, and CRC might recur following surgery and post-surgical treatment[39]. Therefore, regular screening, detection and removal of polyps in the early stages is very important in the prevention of CRC. A systematic review showed that CRC mortality decreased from 8% to 30% in individuals who participated in screening[40]. Thus, people who have risk factors for colon and rectal cancer should be screened regularly. In this study, it was shown that the prevalence of CRC has increased 1.52 times from 2010 to 2019. It has also increased in the world, America and Europe. The prevalence of CRC was higher in men than in women (1.54 *vs.* 1.49). In 2019, 52% of CRC cases were reported in Asian countries. During this period, ASPR of CRC has increased by 17% in men and 11% in women. Considering that ASIR was higher in men than women (11% *vs.* 7%), we can conclude that the prevalence of CRC was also higher in men than in women because more men were diagnosed with CRC. However, it should be kept in mind that the duration of CRC also affects the prevalence of CRC, but we do not know the duration and survival of the disease in men and women. On the other hand, CRC screening programs can also detect cases of the disease that were previously unknown. All in all, the etiology of gender differences in CRC remains uncertain. Some large-scale studies have investigated the role of estrogen and progestin as protective agents against CRC in hormone replacement therapy in postmenopausal women[41,42]. Others have suggested that gender differences could be attributed to different levels of exposure to dietary and lifestyle risk factors[43]. Also, a survey found that men over 50 were particularly unaware of CRC symptoms and the benefits of screening[44], making them less likely to seek medical advice among symptomatic patients and participate in screening programs among asymptomatic individuals. In Turkey, a total of 58.1% of adults stated that they were familiar with screening tests, whereas 65.6% said that they had never had any previous screening tests. Individuals' fecal occult blood test initiation was significantly influenced by variables such as chronic disease, screening tests knowledge, exercise, confidence perception, and barriers[45]. In Asian countries, there are still low screening and verification examination rates due to the absence or insufficient infrastructure, including cancer or death registry systems, colonoscopy capacity, and reasonable subsidization for screening[46]. Onyoh et al[47] found that CRC screening in this region is both effective and cost-effective when compared to no screening at all.

In this study, it was shown that in this time, the number of DALYs of CRC increased by 1.31 times in men and 1.32 times in women. Also, the age-standardized DALY rate has increased by 1% in the entire population, while decreased by 3%, 1% and 7%, in the world, America, and Europe, respectively. Also, the age-standardized DALY rate has increased by 1% in men but remained constant in women. The peak burden of DALY in the entire population, women and men, is in the age group of 65-69 years. Screening potentially reduces the burden of CRC. Screening has been shown to reduce the mortality of CRC by 18% to 57%, depending on the screening test[48]. Therefore, CRC screening plays an important role in reducing its burden. Lifestyle and healthcare services can impact the number of life years lost to cancer. During the 2000s, lifestyle variables were more efficient in cancer, but in recent years, both lifestyle and health service-related variables emerged as effective[38]. There is an urgent need to effectively deal with the alarming rate of CRC. Coordinated efforts will be needed to eliminate modifiable risk factors, leverage chemoprevention research, and promote targeted and widespread population screening to achieve the most significant possible reductions in CRC incidence and mortality. As multiple risk factors contribute to the development of CRC, raising awareness among the general population is critical. Therefore, the effort committed to any strategy must be consistent with the overall health priorities of the specific population, taking financial resources and health care infrastructure into account[49]. This is particularly important as the COVID-19 crisis has had a negative impact on CRC screening and diagnostic programs in recent years[50,51].

CONCLUSIONS

Most of the global burden of CRC occurs in Asian countries, and the increasing trend of incidence, death, prevalence, and burden of this cancer in these countries is faster than in other regions. Therefore, it seems necessary to implement appropriate prevention, diagnosis and treatment strategies in Asian countries to reduce the burden of this disease.

AUTHORS CONTRIBUTIONS:

HS, AM, FR and LA designed and conceived the study. AM collected the data. LA, AM, HS, and FR analyzed and interpreted the data. AM, AR, FR, LA, and HS, drafted the manuscript. HS, FR and AM provided administrative, technical, or material support. All authors contributed to the article and approved the submitted version

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ETHICS APPROVAL:

This study was approved by the Ethics Committee of Jahrom University of Medical Sciences with IR.JUMS.REC.1401.094 code.

INFORMED CONSENT:

In this study, informed consent was not required due to the use of an online database.

AVAILABILITY OF DATA AND MATERIAL:

The data and material used in the current study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST:

All authors declare that they have no conflict of interest.

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