RESEARCH ARTICLE

Gender and Social Disparities in Esophagus Cancer Incidence in Iran, 2003-2009: A Time Trend Province-level Study

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Abstract

Background: Esophagus cancer (EC) is among the five most common cancers in both sexes in Iran, with an incidence rate well above world average. Social rank (SR) of individuals and regions are well-known independent predictors of EC incidence. The aim of current study was to assess gender and social disparities in EC incidence across Iran's provinces through 2003-2009. Materials and Methods: Data on distribution of population at province level were obtained from the Statistical Centre of Iran. Age-standardized incidence rates of EC were gathered from the National Cancer Registry. The Human Development Index (HDI) was used to assess the province social rank. Rate ratios and Kunst and Mackenbach relative indices of inequality (RII_{KM}) were used to assess gender and social inequalities, respectively. Annual percentage change (APC) was calculated using joinpoint regression. Results: EC incidence rate increased 4.6% and 6.5% per year among females and males, respectively. There were no gender disparities in EC incidence over the study period. There were substantial social disparities in favor of better-off provinces in Iran. These social disparities were generally the same between males and females and were stable over the study period. Conclusions: The results showed an inverse association between the provinces' social rank and EC incidence rate in Iran. In addition, I found that, in contrast with international trends, women are at the same risk of EC as men in Iran. Further investigations are needed to explain these disparities in EC incidence across the provinces.

Keywords: Ecological study - esophagus cancer - relative index of inequality - social disparity - trend analysis - Iran

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Introduction

Eliminating health disparities by gender, social class, race/ethnicity and place is considered as a major health policy issue in many countries, both developed and developing. Understanding the current state of health disparities and their causes is a crucial step toward a better understanding of the nature and extent of health disparities and planning to eliminate these disparities. At the same time, it is believed that disparities in cancer incidence and outcomes are a major component of disparities in health (Palmer and Schneider, 2005).

In 2008, an estimated 482,000 new cases of esophagus cancer (EC) were diagnosed worldwide meaning that it was the eighth most common cancer in the world. In the same year, it was the sixth most common cause of death from cancer worldwide (5.4% of the total). In addition, most of these cases (83%) and deaths (86%) occurred in developing world (Ferlay et al., 2010). Previous epidemiological reviews reported substantial variations in incidence of EC within Asia very low incidence in South-West Asia (Salim et al., 2010), low in Peninsular and Island South-East Asia (Moore et al., 2010c), relatively high in North-Western, South and Central Asia (Moore et al., 2010a; 2010b) and high in North-East Asia (Long et al., 2010). In Iran, EC is among the five most common cancers in both sexes with an incidence rate above world average (Kolahdoozan et al., 2010; Moore et al., 2010b). In addition, costal parts of Iran are among areas with high incidence rate in the world (Pickens and Orringer, 2003).

Social rank (SR) of individuals and regions are well-known independent predictor of incidence, diagnosis, treatment and outcomes in cancer context (Weissman and Schneider, 2005). In case of EC, studies reported an inverse association between incidence and mortality rates and SR of individuals and regions (Brown et al., 2001; Weiderpass and Pukkala 2006; Torres-Cintron et al., 2012; Dar et al., 2013; Ljung et al., 2013). In Iran, a previous study conducted in Golestan province with high risk of EC showed an inverse relation between EC incidence and SR (Islami et al., 2009). However, there is a lack of studies in other parts of the country and also how disparities vary over time.

To fill this gap of knowledge, this study examined the distribution of EC incidence rates in Iran using data from cancer registry at province level over years 2003-2009. I focused on following research questions: was there any trend in EC incidence rates over the study period? Were EC

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incidence rates different between men and women? Were these incidence rates associated with the provinces' SR? How these gender and social disparities vary over time? These questions are among policy interests as eliminating health disparities is a common goal of policy-makers in all countries. Moreover, response to these questions is relevant for health resource allocation decisions regarding EC control programs across the provinces in Iran.

Materials and Methods

Study setting

Iran, a lower-middle-income country, is located in the Eastern Mediterranean Region with an area of 1,648,000 km sq. Based on the census data in 2011, a population of about 75 million people are living in Iran.

Data sources and variables

The census and estimated data on the distribution of population at province level were obtained from the Statistical Centre of Iran. Data on age-standardized incidence rate (ASIR) of esophagus cancer per 100,000 population stratified by sex were obtained from published reports by Iran Cancer Registry. By 2007, these reports included only cancer cases diagnosed in pathology departments all over the country which are reported to the Office of Cancer and Genetic Diseases, a subdivision of the Center for Disease Control in the Ministry of Health (Ali Mohagheghi and Mosavi-Jarrahi, 2010). Since 2008, these reports also include non-pathology cases (i.e. population-based registration) to avoid any underestimation in the estimates of cancer incidences (e.g. in 2009, 12.1% of all cancer cases were obtained from non-pathology resources) (Center for Noncommunicable Disease Control, 2012). Human Development Index (HDI) was used as the provinces' social rank (SR) and related data were obtained from the President Deputy of Strategic Planning and Control.

Disparity measures

Two types of disparities were evaluated in the current study: gender and social. For measuring gender disparity, expected number of esophagus cancers incidences was calculated, for both sexes, by multiplying ASIR by population size for each province. Then, female to male rate ratio and its 95% confidence interval was calculated using negative binomial regression with a robust clustered variance to account for data from the same province.

Social inequality was evaluated using Kunst and Mackenbach relative index of inequality (RII_{KM}) (Mackenbach and Kunst, 1997). This is a regression-based measure and takes into account whole population rather than only concentrating on two extreme groups (Mackenbach and Kunst, 1997). To calculate this measure, the provinces were ranked by HDI (from the lowest to the highest) and then the population in each province was assigned a modified ridit-score (a fractional rank) based on the midpoint of range in the cumulative distribution of the population in a given province. For example, if a province with the lowest HDI comprised 10% of the population, a value of 0.05 (0.1/2) is assigned to this province, and if second province comprise 15% of population, a value of 0.175 (0.1± [0.15/2]) is assigned to this province and so forth. Then, the expected number of cancer incidences in the provinces was regressed on these fractional ranks using negative binomial regression with a robust variance and population as exposure variable. With the lowest SR as reference, an RII_{KM} value greater (lesser) than 1 show that ASIR was higher among provinces with higher (lower) SR (more distance from 1 implies more disparity). Actually, in this case, RII_{KM} has an interpretation similar to risk ratio or relative risk. Excel office and STATA version 11 were used for these analyses. In addition, to test if social disparities are different between women and men and between the first and the last year of the study, I used suest command in STATA to compare estimated regression coefficients.

To examine changes of ASIR over time, I calculated annual percentage change (APC) and its 95% confidence interval for both sexes using the Joinpoint Regression Program 3.5.4. Moreover, to examine if there were differences in changes of ASIR over time across social groups, the provinces were ranked and divided in five quintiles by HDI (weighted by their population) and APCs and its 95% confidence intervals for these quintiles were calculated using the same software.

Results

Figures 1 present average ASIR of esophagus cancer per 100,000 population among females and males over study period in Iran's provinces. It can be seen that there were substantial differences in the distribution of esophagus cancer incidences across the country and it was more prevalent in the north of the country. Among females, Kordestan and Chaharmahal Bakhtiari provinces had the highest and the lowest ASIR during study period,

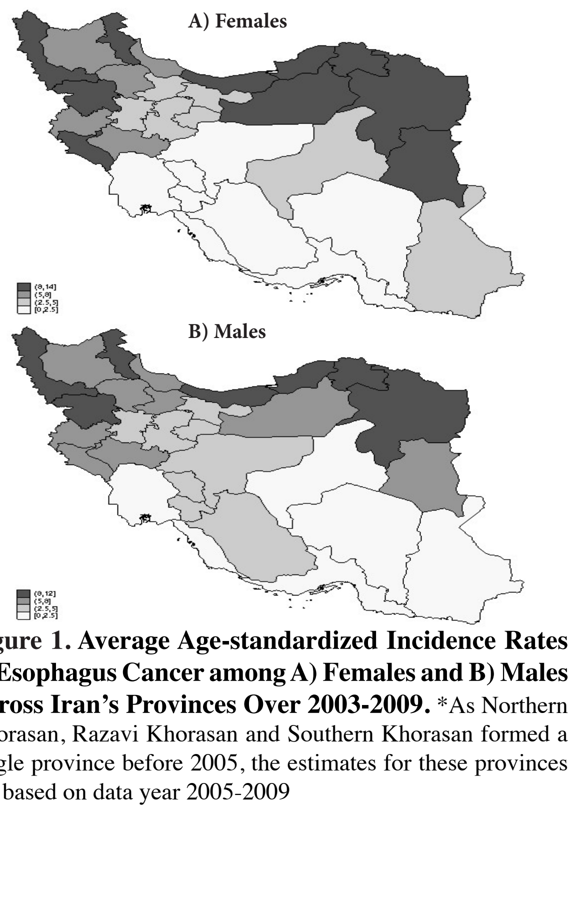

Figure 1. Average Age-standardized Incidence Rates of Esophagus Cancer among A) Females and B) Males Across Iran's Provinces Over 2003-2009. *As Northern Khorasan, Razavi Khorasan and Southern Khorasan formed a single province before 2005, the estimates for these provinces are based on data year 2005-2009

Table 1. Gender and Social Disparities of Esophagus Cancer Incidences in Iran, 2003-2009

Measure	Female to Male rate ratio (95%CI)	Relative index of inequality (95%CI) Females	Males	Equality of coefficients between Females and males
2003	1.12 (0.97-1.29)	0.41 (15-1.07)	0.65 (0.27-1.56)	0.05
2004	1.09 (0.92-1.30)	**0.20 (0.10-0.43)**	**0.44 (0.21-0.95)**	0.02*
2005	1.23 (0.96-1.57)	0.29 (0.08-1.04)	**0.23 (0.11-0.48)**	0.7
2006	1.01 (0.91-1.12)	**0.23 (0.09-0.56)**	**0.34 (0.17-0.70)**	0.03*
2007	0.93 (0.83-1.06)	**0.35 (0.17-0.70)**	**0.36 (0.18-0.72)**	0.91
2008	1.03 (0.93-1.14)	**0.31 (0.13-0.73)**	**0.41 (0.20-0.85)**	0.16
2009	0.96 (0.85-1.08)	**0.31 (0.18-0.54)**	**0.26 (0.14-0.48)**	0.44

*RII was statistically different between females and males: **Bold figures display a statistically significant result (p<0.05)

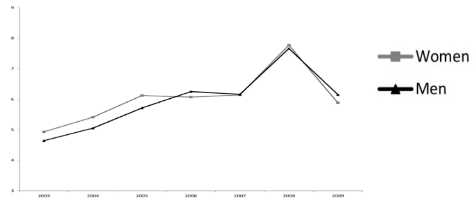

Figure 2. Age-standardized Incidence Rates of Esophagus Cancer Over 2003-2009, Stratified by Sex

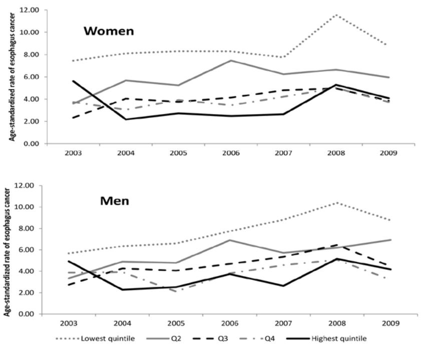

Figure 3. Age-standardized Incidence Rates of Esophagus Cancer Across Five Quintiles of HDI Over 2003-2009, Stratified by Sex

respectively (17.5-fold difference). Among males, Razavi Khorasan and Hormozgan provinces had the highest and the lowest ASIR during study period, respectively (12-fold difference). Figure 2 shows overall ASIR for females and males over study period. Trend analysis showed that for females, APC was 4.6% and marginally significant (p=0.08) and for males, ASIR increased 6.5% per year at the same time period (p=0.02). While in the most years females had a higher ASIR than males, however these differences were not statistically significant implying no gender disparity in incidence of esophagus cancer in Iran (Table 2 column 2). Figures 3 show the distribution of ASIR across five quintiles of HDI among females and males over the study period. In both sexes, provinces in the lowest quintile of HDI had higher ASIR than provinces with a better HDI position. Trend analysis revealed that only men in the three lowest quintile of HDI experienced a significant increase at ASIR over the study period and APC was not statistically significant among the two highest quintiles of HDI in men and all the five quintiles in women.

The results of RII_{KM} showed that, among both sexes, provinces with lower HDI had generally a higher risk of EC incidence implying social disparities in the country in favor of better-off provinces. For both sexes, there were no statistically significant differences in RII_{KM} values between 2003 and 2009. The last column at Table 2 shows results of test of equality of RII_{KM} between males and females and highlights that only in 2 out of 7 years, social disparity was more profound among females than males. In remaining 5 years, there were no statistically significant differences in RII_{KM} values between men and women.

Discussion

In this study, for the first time, I assessed gender and social disparities in the distribution of EC incidence across the Iran's provinces over a period of seven years (2003-2009). EC incidence rates increased in both sexes over the study period. The findings indicated that there were no significant gender disparities in the study years. I found, for both sexes, profound social disparities in the distribution of EC incidence rates across the country in favor of better-off provinces. In addition, there were no statistically significant differences in social disparities by sex and time.

EC incidence rose by 6.5% (males) and 4.6% (females) per year for the period 2003 to 2009. This increase in incidence over time is in line with studies from the United States (Simard et al., 2012) and Canada (Otterstatter et al., 2012). Obesity and gastro esophageal reflux disease (GERD) are two established risk factors for EC (Lagergren et al., 1999a; 1999b). Recent studies showed that both these risk factors increased in Iran over recent years (Esteghamati et al., 2010; Sepanlou et al., 2010) and this might partly explain increasing trend in EC incidence in the current study. In addition, improving and expanding cancer registry from histological confirmed cases to population-based registry might be another potential explanation for the observed trend in my study.

I did not find any gender disparity in EC incidence rate over the study period. While in most countries EC incidence rate is higher among males than females (Ferlay et al., 2010), it is well-known that in high incidence areas like Iran, male to female ratio is equal or even excess female cases are observed (Melhado et al., 2010). Similar finding was observed in Pakistan (Moore et al., 2010a). On the other hand, inverse association between EC incidence rate and SR in the current study is in line with previous individual and ecological studies (Brown et al., 2001; Singh et al., 2002; Weiderpass and Pukkala, 2006; Torres-Cintron et al., 2012; Jansson et al., 2005; Dar et al., 2013; Ljung et al., 2013). It is argued that risk factors of EC such as smoking, low consumption of fruit and vegetables and obesity are more prevalent among people and areas with low SR (Ellaway et al., 1997; Dubowitz et al., 2008; Hiscock et al., 2012; Di Cesare et al., 2013). Inverse associations between SR and these risk factors have been also reported in Iran (Dastgiri et al., 2006; Mehrabi et al., 2007; Kiadaliri, 2013). Higher prevalence of these risk factors among people and provinces with lower SR might partly explain observed inverse association between EC incidence and SR in the current study. Similar to a previous finding among men in Finland (Weiderpass and Pukkala, 2006), I found that these social disparities in EC incidence were stable over time. This finding implies that possibly social disparities in distribution of risk factors have been stable over time in the country. In addition, it means that policies and interventions to eliminate these social disparities either have not been conducted or have not been effective and imply necessity of initiating new policies and promote effectiveness of current policies in the country. In line with a previous study in Iran (Mohebbi et al., 2011), I did not find any significant difference in social disparity between men and women in most years of the study. This was observed because mean and distribution of EC incidence rates were similar in four out of five quintiles of HDI and there were similar trends in EC incidence among both sexes. It should be noted that due to ecological nature of the study and in turn the same distribution of HDI for both sexes, this result should be considered with caution. Further analyses, especially examining social disparity in EC risk factors by sex, are required to provide more insight regarding this finding.

The findings of the current study should be interpreted in light of some limitations. Firstly, there is the issue of error in the recording and classification; especially in pathology registries might be a source of bias. I expect that this is more common in the provinces with lower social rank; therefore, it is suggested that the social disparity might be more profound than what has been reported here. Secondly, national cancer registry data provide data at the province-level which did not allow analysis for smaller geographic areas such as counties. This implies that the observed disparities in EC incidence are between-provinces and these are not necessarily applicable to smaller geographic units or individuals. Thirdly, no causal inference can be drawn due to ecological nature of the study and that there was no control for confounders (e.g. lifestyle factors) in this study.

In conclusion, the present study indicated that there has been an increasing trend in EC incidence among men and women in Iran through 2003-2009. It was shown that there were substantial social disparities in the distribution of EC incidence across the provinces in Iran in favor of better-off provinces. In addition, I found that, in contrast with international trend, women are at the same risk as men in Iran. Further investigations are needed to explain these disparities in EC incidence across the provinces and also on the smaller geographical units and at the individual level in order to design better EC control program.

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