Disparities in incidence and mortality of pancreatic cancer in the world

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Abstract

Background: Pancreatic cancer (PC) is as the twelfth most frequent cancer and the seventh most important cause of mortality by reason of cancer in the world. Being informed about the incidence and mortality of this cancer and the potential role of development is useful in health policy. The aim of this research is investigating disparities in the incidence and mortality of PC in the world countries in the year 2012. Methods: This study was an ecologic study in the World for assessing the correlation between Human Development Index (HDI) and its details (Gross national income (GNI) per capita, average years of schooling and life expectancy at birth) with age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC. Results: In total, 337872 new cases of PC occurred in 2012 around the world, that 178116 and 159711 cases take happen in men and women respectively, also at the same year 330391 deaths of PC occurred, that 173,827 and 156564 cases were in men and women. In assessment the relationship between HDI and ASIR and ASMR of PC there is significant positive correlation equal to 0.767 (p <0.001) between HDI and ASIR of PC, and a significant positive correlation equal to 0.776 (p <0.001) between HDI and ASMR of PC.
Conclusion: The incidence and mortality of PC has a significant positive correlation with the Human Development Index.

Keywords
Disparities, Incidence, Mortality, Pancreatic cancer, World

Introduction
Gastrointestinal cancers have high incidence and mortality rate worldwide (Jemal et al., 2010a; Siegel et al., 2012). Pancreatic cancer (PC) is one of the cancers that is identified as the twelfth common cancer and the seventh death cause due to cancer worldwide so that its incidence was 12.2 and death due to that was 10.9 per hundred thousand people in 2014 (Howlader et al., 2011). The highest incidence of PC is observed in Northern Europe and America and the lowest incidence is seen in African countries (Altekruse et al., 2010; Curado et al., 2007; Malvezzi et al., 2013; Pakzad et al., 2016). Totally, 2/3 of PC death cases occur in world developed countries (Parkin et al., 2005). Therefore it's known as the fifth deadly cancer in developed countries in 2000 (Schwartz and Reis, 2000).

Despite the diagnosis of more than 400000 PC new cases in year, it is about 30 years that its 5-year survival remains low and less than 4 percent is reported for this cancer (Baxter et al., 2007; Jemal et al., 2010b; Stats, 2012). The global burden of PC is increasing due to aging, population growth and high-risk behaviors especially smoking and world developed countries allocated the greatest burden of the disease (Jemal et al., 2011). As the country is more advanced and has higher-income, non-communicable diseases such as cancers include more death causes (Mathers et al., 2005). However, the cause of incidence and prevalence of PC is due to its risk factors including age over 70, smoking, race, obesity, alcohol, red and processed meat consumption, chronic pancreatitis, diabetes and chronic infections (hepatitis B, hepatitis C, Helicobacter pylori) different distribution that is believed to be higher in developed countries (Keane et al., 2014; Lowenfels and Maisonneuve, 2006; Society, 2013). The society health is the outcome of several complex, different and constantly changing factors (Organization, 2000). So, it should be cared, intervened and managed and be in the place of social and economic development level, continuously (Organization, 2000). Therefore, one of the good public health and its related factors indicator is the Human Development Index (HDI) (Bray et al., 2012). This index is a useful classification for cancer globalization (Bray et al., 2012). The HDI was determined as a comparing index for countries in 3 fields of human dimension by the UNDP (United Nations Development Program) in 1990 (Ravallion, 1997). Three dimensions of HDI
include long and healthy life, access to knowledge and good living standards (Bray et al., 2012). Each of these factors are measured by life expectancy at birth, education and GDP per capita, respectively (Bray et al., 2012).

An estimated 5-year incidence of all cancers according to HDI regions showed that areas with high and very high HDI, have allocated highest prevalence of 21.31% to themselves despite having only 6.1% of the world's population and this ratio was 9.237% and 1.993 % for medium and low HDI regions, respectively (Bray et al., 2013).

PC among other cancers has different incidence and mortality that varies around the world and it is due to development and the diagnostic and therapeutic status of countries (Bray, 2014; Forman et al., 2014; Franceschi and Wild, 2013; Kanavos, 2006).

However, a comprehensive study that could examine the association between HDI and age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC has not been conducted. Because of this point that knowledge about the ASIR and ASMR of cancers and the potential role of development is useful in health planning, this study conducted with the purpose of determining the ASIR and ASMR of PC and its correlation with the HDI in the world in 2012.

**Materials-Methods**

This study was an ecologic study in the World for assessing the correlation between HDI and its details (Gross national income (GNI) per capita, average years of schooling and life expectancy at birth) with age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC. Detailed descriptions of the methods used in collection of data about cancer incidence and mortality in GLOBOCAN (Ferlay J et al., 2016), and HDI (Malik, 2013), and Statistical analysis of this study have been provided in previous reports (Arabsalmani et al., 2017; Ghoncheh et al., 2016; Hassanipour-Azgomi et al., 2016; Mohammadian et al., 2017; Raﬁemanesh et al., 2016; Razi et al., 2016; Shuja et al., 2017; Tiyuri et al., 2017).

**Results**

**The frequency of incidence of PC**

In total, 337872 PC cases have been occurred worldwide in 2012 that 178161 and 159711 cases were in men and women respectively (Sex Ratio = 1.11). From all occurred cases, about 174344 cases were in countries with very high HDI,
55638 cases were in countries with high HDI, 98632 cases were in countries with medium HDI, and 9108 cases occurred in countries with low HDI. Five countries with the heights sum of PC include: China (65727), America (42885), Japan (32899), Germany (16451) and Russia (14512). Five countries with highest sum of PC case in men include: China (39299), America (21713), Japan (17013), Germany (7972) and Russia (7206), and in women include: China (26428), America (21172), Japan (15886), Germany (8479), and Russia (7306).

**The ASIR of PC**

The ASIR of PC per hundred thousand people in the world was 4.2 (in men 4.9 and in women 3.6). The ASIR of PC in very high HDI regions was 7.2, in high HDI regions was 4.6, in medium HDI regions was 2.7, and in low HDI regions was 1.2. Five countries with the highest ASIR of PC are: Czech Republic (9.7), Slovakia (9.4), Armenia (9.3), Hungary (9.3), and Slovenia (8.8), respectively. 5 countries with the highest ASIR of PC for men were: Armenia (11.9), Czech Republic (11.9), Slovakia (11.5), Hungary (11.5), and FYR Macedonia (11.5), and in women include: Czech Republic (7.9), Slovenia (7.8), Slovakia (7.8), Denmark (7.7), and Finland (7.6).

**The frequency of mortality of PC**

Nowadays, 330391 deaths happened because of PC around the world in 2012 that about 173827 cases were men and 156564 cases were women (Sex Ratio = 1.11). Total number of mortality from PC was 170497 cases in very high HDI region, 56474 cases in high HDI region, 94447 cases medium HDI region, and 8822 cases in low HDI region. Five countries having the highest ASMR of PC were: China (63662), America (41509), Japan (31046), Russia (16371), and Germany (16188). Five countries having the highest ASMR of PC in men were: China (37775) cases, America (21005), Japan (15809), Russia (8168), and Germany (7900), and in women include: China (25887), America (20504), Japan (15237), Germany (8288), and Russia (8203).

**The ASMR of PC**

The ASMR of PC per hundred thousand people in the world was 4 (in men 4.7 and in women 3.4). The ASMR of PC very high HDI regions was 6.8, in high HDI regions was 4.6, in countries with medium HDI regions was 2.6, in low HDI regions was 1.2. Five countries having the highest ASMR of PC per hundred thousand people were: Armenia (8.9), Hungary (8.8), Czech Republic (8.7), Slovakia (8.5), and French Guiana (8.1). Five countries having the highest ASMR of PC in men were: YR Macedonia (11.8), Armenia (11.6), Hungary (11.1), Estonia (10.6), and Latvia (10.4), and in women include: Slovakia (7.6), Czech Republic (7.2), Slovenia (7.2), Hungary (7), and French Guiana (7).

**The association between the ASIR of PC and the HDI**
In assessment the relationship between ASIR of PC and the HDI, a significant positive correlation equal to 0.767 (p < 0.001) was observed. There were positive correlation between ASIR of PC and components of the HDI (with the level of income equal to 0.517 (p < 0.001), with average years of education equal to 0.762 (p < 0.001) and with life expectancy at birth equal to 0.657 (p < 0.001) (Fig. 1).

![Figure 1](image1.png)

**Figure 1. The relationship between standardized incidence rate and the Human Development Index.**

The association between the ASMR of PC and the HDI

In topic of the relationship between ASMR of PC and the HDI, a significant positive correlation equivalent to 0.776 (p < 0.001) was observed. There were positive correlation between ASMR of PC and components of the HDI (with the level of income equal to 0.518 (p < 0.001), with average years of education equal to 0.769 (p < 0.001) and with life expectancy at birth equal to 0.666 (p < 0.001) (Fig. 2).

![Figure 2](image2.png)

**Figure 2. The relationship between standardized mortality rate and the Human Development Index.**
Discussion

PC has allocated the mortality rate of 39.4 and incidence rate of 54.9 cases per 100,000 people of the population to itself in 2008 (Hu et al., 2013). Also, according to a cohort study that has been conducted in 2000-2010, incidence of PC has increased 3% annually (Keane et al., 2014).

In this study, ASIR of PC was estimated 4.2 per hundred thousand people in the world and has a positive correlation of 0.767 with the HDI that this association is statistically significant. Czech Republic, Slovakia, Armenia, Hungary and Slovenia were 5 countries that allocated the highest rate of incidence to them. This is in condition that every five country is located in group of countries with high and very high HDI.

According to studies, the incidence of PC in industrial developed countries is more than developing ones. In a systematic study which Rio conducted in 1975-2007, it's estimated that the highest incidence of PC belongs to Northern Europe and America (Altekruse et al., 2010). Estimating incidence age specified rates (ASRs) is 10.1 for both sexes per hundred thousand people based on gender in Europe in 2012 (Ferlay et al., 2013). While, the same rate is estimated to be 3.2 per hundred thousand people in Asia in 2012 (Pourhoseingholi et al., 2014).

The diseases incidence is associated with their risk factors (Ward et al., 2004). Age and smoking are strong factors that always are reported (Bonelli et al., 2003; Fuchs et al., 1996; Hassan et al., 2007; Hippisley-Cox and Coupland, 2012; Larsson et al., 2005; Muscat et al., 1997; Silverman et al., 1994; Stapley et al., 2012; Valean et al., 2015). So that by increasing the number of years of life that passes by smoking cigarettes, the risk to catch PC also boost per person (Keyghobadi et al., 2015). Variety diet could be mentioned that other risk factors. Also several studies have shown that the total amount of calorie and probably fat increase in the diet and obesity, may arise the risk of PC (Ghadirian et al., 1990). Finally, we can say that the high level of these factors in developed countries has led to a greater incidence of PC.

The ASMR of PC was 4 per hundred thousand people in the world in this study and a positive correlation of 0.776 was seen between ASMR of PC and the HDI that this was statistically significant. 5 countries having the highest ASMR of PC are: Armenia, Hungary, Czech Republic, Slovakia, and French Guiana. So that Armenia and French Guiana are located in group of countries with high HDI and three other ones in countries with very high HDI.

Also, due to the results of studies that have been conducted between the years 1993-95, it's estimated that PC was the sixth cause of death among cancers in the United States of America and the United Kingdom (Berman, 1995; Gold and Goldin, 1998). Also in 2002, according to cancer mortality in the world, the incidence of PC is estimated to be 6-8 per 100 thousand people in men and 4-6
per 100 thousand people in women in developed countries such as Australia and Japan (Parkin et al., 2005).

In many Asian countries such as Korea, Singapore and China that have a high HDI, PC mortality is high too (Parkin et al., 2005; Wang et al., 2003).

In this study, the incidence in men is 4.9 and in women is 3.6 per hundred thousand people and the mortality is 4.7 for men and 3.4 per hundred thousand in women.

However, in all cancer centers an association is reported between PC and gender (Bramhall et al., 1995). The prevalence of this disease in men is more than women (Bramhall et al., 1995). So that due to global estimation in 2012, the rate of mortality to incidence of cancer in both sexes is almost close (0.94 / 0.97) (Valean et al., 2015). Although the incidence in men is generally a little more than women, the high incidence and mortality of PC in men has a variety of causes such as increase in smoking (Muniraj et al., 2013), diet (high fat and protein, low fruit and vegetable consumption), consumption of coffee, alcohol and Job hazards (insecticides, aluminum, nickel and acrylamide) that these things cases are seen more in men's lifestyle (Greene et al., 2008; Lowenfels et al., 1997). While, elevated estrogen in women acts as a death cause lowering agent of PC (Greene et al., 2008).

In this study, a positive correlation was observed between the ASIR and ASMR of PC and life expectancy at birth. Also it has been seen in several studies that with increasing age, the incidence of PC dramatically raised up increases (Ferlay et al., 2015; Hartwig et al., 2009; Neesse et al., 2010; Sasson et al., 2002; Toriola et al., 2014). So that the cause for increasing incidence of this cancer in developed countries, may be a reflection of aging (Pakzad et al., 2015c; Smith et al., 2009). In this study, a significant positive correlation was seen between the ASIR and ASMR of PC with mean education level. Also in Bosetti et al study, the incidence is increased with increasing level of education (Bosetti et al., 2012). Also about the PC mortality, the mortality is increased in less educated individuals with age under 15 years (Jemal et al., 2013).

In this study, a significant positive correlation was seen between the ASIR and ASMR of PC with average income level. According to several studies, patients with high socio-economic status and PC have good chance for surgical treatment but has no significant impact on patient survival (Bakens et al., 2015; Michaud, 2004; Pakzad et al., 2015a, b). Surgery as the only treatment option for long-term survival in patients with PC as an indicator of the impact of social and economic inequality, is a good witness that socioeconomic status has the lowest effect on patient's survival (Bakens et al., 2015; Michaud, 2004). Because the average survival of PC is 3-6 months since diagnosis without treatment that has up to 23 months increase after surgery and adjunctive therapies (Neoptolemos et al., 2001; Neoptolemos et al., 2010). That’s why we can say that the incidence of PC is near to its mortality rate (Michaud, 2004; Ryu et al., 2010). Although in
several studies observed that patients with higher income have more improvement than others, but this improvement is very low. Therefore, we cannot consider its protective effects very important (Neoptolemos et al., 2001; Neoptolemos et al., 2010).

**Conclusion**

We can say that, the incidence and mortality of PC has a significant positive correlation with the Human Development Index and its components.

**Abbreviations**

- ASIR: Age-Standardized Incidence Rate
- ASMR: Age-Standardized Mortality Rate
- HDI: Human Development Index
- PC: Pancreatic cancer

**Author Contribution**

All authors contributed to the design of the research. Y KH, M A, R P, and M GH extracted the data and summarized it. All authors drafted the first version. Y KH, A MH and HS edited the first draft. All authors reviewed, commented and approved the final draft.

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