Favorable Lip and Oral Cancer Mortality-To-Incidence Ratios in Countries With High Human Development Index and Expenditures On Health

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Abstract

Background: The incidence rate of lip and oral cancer is increasing in recent years, the prognosis of which is associated with a country's socioeconomic status. The mortality-to-incidence ratio (MIR) is a reasonable indicator of disparities in cancer screening and treatment. We aim to understand the association between economic status and cancer prognosis.

Methods: Data were obtained from the Global Cancer Observatory (GLOBOCAN) and the World Health Organization (WHO). The MIR was applied to evaluate the correlation to healthcare expenditures and the human development index (HDI) disparities via Spearman's rank correlation coefficient.

Results: The results showed that Asia has the most cases and deaths. The association of the HDI, current health expenditure (CHE), and ratio of CHE to the percentage of gross domestic product (CHE/GDP) to the crude rate (CR) of incidence show significant results ($p < 0.001$, $p = 0.005$, and $p < 0.001$, respectively). However, their association with the mortality rate ($p = 0.303$, $p = 0.997$, and $p = 0.101$) is not significant. In the correlation of the MIRs, the results revealed a significant association with the HDI, CHE, and CHE/GDP with the MIR ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively).

Conclusion: Countries with a higher HDI, more CHE per capita, and higher CHE/GDP tend to have a lower MIR, which indicates a favorable clinical outcome.

Introduction

Lip and oral cancer is one of the most common cancers worldwide, and the incidence rate has increased continuously in recent years [1]. South Asia and Southeast Asia has the most cases [2]. Among all anatomic subsites of lip and oral cavity cancer, the tongue is the most common affected site worldwide, and buccal/labial mucosa is the second most common affected site in Asia [3]. The most common risk factors of lip and oral cavity cancer include tobacco, alcohol, betel quid, Epstein-Barr virus and human papillomavirus infection [4, 5]. Oral cavity cancer can be diagnosed early at a lower stage with leukoplakia by visual examination, biopsy or image study; thus, early oral screening is beneficial [6]. However, poor and less educated people with risk factors seldom obtain a screening of oral cancer; thus, diagnosis is usually delayed for these people [7].

Standard treatment of oral cancer includes surgical resection, radiotherapy, chemotherapy or a combination of them, depending on their stages [8]. A previous study indicated that over the past forty years, the prognosis of oral cancer had substantially improved particularly due to the application of adjuvant therapy and adjuvant chemoradiotherapy [9]. Recently, immunotherapy has emerged as a potential and effective treatment [8, 10]. The prognosis of oral cancer is related to several factors, such as race [11] and anatomic subsites [12]. Moreover, the early detection of oral cancer is one of the most important factors that affect the overall survival and prognosis [13], since an affordable examination target to oral cancer can help early diagnosis and improve the prognosis and survival rate [14], and the prognosis has disparities in socioeconomic status [15]. People with limited income may receive much less definitive therapy and have much more burden from oral cancer and worse overall survival rates [16, 17].

The mortality-to-incidence ratio (MIR), which is calculated by normalizing crude mortality rates to its incidence, which determines whether a country has a higher mortality or a lower mortality [18], reveals the overall mortality

rate after diagnosis of the disease [19]. Previous studies, such as a study by Sunkara & Hébert [20], suggested that the MIR could be a useful indicator to identify the regional disparities in cancer screening and treatment.

As MIR presents mortality after accounting for incidence, it can help us assess the burden and prognosis of cancer. Thus, in this study, we evaluate health expenditures, the human development index (HDI), and MIRs of different countries and aim to understand the association between economic status and cancer prognosis.

Materials And Methods

Lip and oral cavity cancer, ICD-10 C00-06, epidemiological data were obtained from the Global Cancer Observatory (GLOBOCAN) database (<https://gco.iarc.fr/today/>), which is a public access database that provides contemporary estimates of cancer epidemiology for 185 countries in 2018. The HDI was obtained from the United Nations Development Programme, Human Development Report Office (<http://hdr.undp.org/en>). The data on health expenditures, including the per capita current health expenditure (CHE) and ratio of CHE to the percentage of gross domestic product (CHE/GDP), were obtained from the World Health Statistics database (https://www.who.int/gho/publications/world_health_statistics/en/).

The MIR was defined as the ratio of the crude rate (CR) of mortality to the CR of incidence, as previously described [20-23]. The exclusion criteria for country selection were based on the missing data of the World Health Organization (WHO) statistics (N=12), missing data of the HDI (N=2), and data quality report of the GLOBOCAN (N=110, [24]). A total of 61 countries were included in the final analysis. Associations between the MIR and other factors among various countries were estimated using Spearman's rank correlation coefficient, which was calculated using SPSS statistical software version 15.0 (SPSS, Inc., Chicago, IL). The values of $p < 0.05$ were considered statistically significant. Scatterplots were generated with Sigma Plot.

Result

Epidemiology of lip and oral cancer according to the regions

We survey 339,913 new cases and 168,169 deaths of lip and oral cavity cancer in this study. The rank and percentage of lip and oral cavity cancer in all cancers of selected regions and cumulative risk are shown in Table 1. The incidence rates by regions are Africa (13,324), Asia (220,810), Europe (57,737), Latin America and the Caribbean (18,525), North America (25,354), and Oceania (4,163). The number of deaths by region are Africa (9,066), Asia (124,900), Europe (21,834), Latin America and the Caribbean (7,050), North America (4,424), and Oceania (895). Among all selected regions, Asia has the most cases and deaths as well as the highest percentage among all cancers. Conversely, Oceania has the fewest cases and deaths.

Table 1. Summary of the number, crude rank, ASR and MIR of lip and oral cancer by region.

Region	New cases			Deaths			
	Number	CR	ASR	Number	CR	ASR	MIR
Africa	13324	1.0	1.7	9066	0.7	1.2	0.71
Asia	220810	4.9	4.2	124900	2.8	2.4	0.57
Europe	57737	8.0	4.3	21834	3.0	1.6	0.38
Latin America and the Caribbean	18525	2.9	2.6	7050	1.1	1.0	0.38
North America	25354	7.1	4.2	4424	1.2	0.7	0.17
Oceania	4163	10.2	7.5	895	2.2	1.5	0.22

Epidemiology and parameters of the development and health expenditure of lip and oral cancer of the selected countries

The HDI, CHE, cancer incidence, cancer mortality, and MIR of selected countries are shown in Table 2. Norway has the highest HDI (0.954), and Egypt has the lowest HDI (0.700). The electronic GDP (e-GDP) ranges from 3.1% (Qatar) to 16.8% (United States of America). According to the incidence rates among all countries that were examined, Qatar and Bahrain have the lowest CR (1.0), and Chile has the lowest age standardized rate (ASR, 1.1), Latvia has the highest crude rates (12.7 of CR) and Australia has the highest ASR (6.9). Latvia has the highest mortality CR (6.0), and Egypt has the lowest mortality CR (0.4), while Latvia has the highest ASR (3.2) and Chile, Egypt, Israel, Malta and Jamaica have the lowest ASR (0.4). Australia has the lowest MIR (0.14), and Bahrain has the highest MIR (0.64).

Table 2. Summary of HDI, CHE, cancer incidence, cancer mortality, and MIR in lip and oral cancer (N=61).

Country	HDI	CHE		Incidence			Mortality			
		Per Capita	% of GDP	Number	CR	ASR	Number	CR	ASR	MIR
Argentina	0.830	998	6.8	1357	3.1	2.5	512	1.2	0.9	0.39
Australia	0.938	4934	9.4	2682	11.1	6.9	378	1.6	0.9	0.14
Austria	0.914	4536	10.3	488	5.7	3.0	232	2.7	1.4	0.47
Bahrain	0.838	1190	5.2	16	1.0	1.5	10	0.6	1.0	0.64
Belarus	0.817	352	6.1	653	7.0	4.1	316	3.4	2.0	0.49
Belgium	0.919	4228	10.5	923	8.3	4.7	305	2.7	1.4	0.33
Brazil	0.761	780	8.9	9902	4.7	4.0	3965	1.9	1.6	0.40
Bulgaria	0.816	572	8.2	459	6.7	3.4	164	2.4	1.2	0.36
Canada	0.922	4508	10.4	2633	7.3	3.9	594	1.6	0.8	0.22
Chile	0.847	1102	8.1	275	1.5	1.1	113	0.6	0.4	0.42
Colombia	0.761	374	6.2	775	1.6	1.4	308	0.6	0.5	0.39
Costa Rica	0.794	929	8.1	78	1.6	1.2	35	0.7	0.5	0.44
Croatia	0.837	852	7.4	291	7.2	3.8	117	2.9	1.5	0.40
Cuba	0.778	826	10.9	1238	11.0	6.2	380	3.4	1.8	0.31
Cyprus	0.873	1563	6.8	29	2.5	1.6	8	0.7	0.5	0.27
Czechia	0.891	1284	7.3	859	8.3	4.3	361	3.5	1.8	0.42
Denmark	0.930	5497	10.3	397	7.1	3.8	125	2.2	1.1	0.31
Ecuador	0.758	530	8.5	217	1.3	1.2	82	0.5	0.5	0.38
Egypt	0.700	157	4.2	1295	1.3	1.6	352	0.4	0.4	0.28
Estonia	0.882	1112	6.5	79	6.2	3.3	40	3.1	1.7	0.50
Fiji	0.724	175	3.6	27	3.0	2.9	11	1.2	1.2	0.40
Finland	0.925	4005	9.4	348	6.5	3.0	116	2.2	0.9	0.34
France	0.891	4026	11.1	6815	10.8	6.2	1516	2.4	1.3	0.22
Germany	0.939	4592	11.2	7271	9.1	4.4	2311	2.9	1.3	0.32
Iceland	0.938	4375	8.6	13	3.9	2.3	3	0.9	0.5	0.23
Ireland	0.942	4757	7.8	275	5.8	3.7	74	1.6	0.9	0.28
Israel	0.906	2756	7.4	155	1.9	1.4	51	0.6	0.4	0.32
Italy	0.883	2700	9.0	3500	6.1	2.7	1184	2.1	0.9	0.34
Jamaica	0.726	294	5.9	52	1.8	1.5	15	0.5	0.4	0.29

Japan	0.915	3733	10.9	8138	6.7	2.8	2496	2.1	0.7	0.31
Kuwait	0.808	1169	4.0	59	1.4	2.0	33	0.8	1.1	0.56
Latvia	0.854	784	5.8	239	12.7	6.8	113	6.0	3.2	0.47
Lithuania	0.869	923	6.5	188	6.7	3.7	114	4.1	2.3	0.61
Luxembourg	0.909	6236	6.0	45	7.8	4.8	10	1.7	1.0	0.22
Malaysia	0.804	386	4.0	640	2.0	2.0	302	1.0	1.0	0.48
Malta	0.885	2304	9.6	18	4.2	1.9	6	1.4	0.4	0.33
Mauritius	0.796	506	5.5	62	4.9	3.3	28	2.2	1.5	0.45
Netherlands	0.934	4746	10.7	1418	8.5	4.4	257	1.5	0.7	0.18
New Zealand	0.921	3554	9.3	264	5.7	3.4	58	1.2	0.7	0.21
Norway	0.954	7464	10.0	362	6.9	3.7	68	1.3	0.7	0.19
Oman	0.834	636	3.8	65	1.3	2.0	31	0.6	1.1	0.49
Philippines	0.712	127	4.4	1372	1.3	1.6	673	0.6	0.8	0.48
Poland	0.872	797	6.3	3203	8.6	4.8	1505	4.0	2.2	0.47
Portugal	0.850	1722	9.0	817	8.2	4.3	269	2.7	1.4	0.33
Qatar	0.848	2030	3.1	26	1.0	2.0	14	0.5	1.4	0.54
Russian Federation	0.824	524	5.6	9340	6.6	4.0	5443	3.8	2.3	0.58
Serbia	0.799	491	9.4	701	8.1	4.9	261	3.0	1.7	0.37
Singapore	0.935	2280	4.3	199	3.5	1.9	85	1.5	0.8	0.43
Slovakia	0.857	1108	6.9	541	10.1	6.0	224	4.2	2.5	0.42
Slovenia	0.902	1772	8.5	135	6.7	3.5	47	2.3	1.1	0.34
South Africa	0.705	471	8.2	1328	2.3	2.7	829	1.4	1.7	0.61
South Korea	0.906	2013	7.4	1467	2.9	1.6	507	1.0	0.5	0.34
Spain	0.893	2354	9.2	3843	8.6	4.0	969	2.2	1.0	0.26
Sweden	0.937	5600	11.0	556	5.7	2.8	145	1.5	0.7	0.26
Switzerland	0.946	9818	12.1	639	7.7	4.0	184	2.2	1.1	0.29
Thailand	0.765	217	3.8	4169	6.1	3.8	2159	3.2	2.0	0.52
Trinidad and Tobago	0.799	1146	6.0	42	3.1	2.2	20	1.5	1.1	0.48
Ukraine	0.750	125	6.1	3358	7.8	4.4	2058	4.7	2.8	0.60
United Kingdom	0.920	4356	9.9	5645	8.7	4.9	1443	2.2	1.1	0.25
United States of	0.920	9536	16.8	22715	7.1	4.2	3830	1.2	0.7	0.17

America										
Uruguay	0.808	1281	9.2	149	4.4	2.9	70	2.1	1.3	0.48

Association between MIR and parameters of the development and health expenditure of the selected countries

We further examined the association between the HDI, CHE and CRs of incidence and mortality (Fig 1). The association between HDI and CR of incidence ($p<0.001$, Figs 1A) yields significant results, while mortality ($p=0.303$, Figs 1B) does not yield significant results. On the other hand, the incidence of CHE to CR and CHE/GDP to CR show significant results ($p=0.005$, Figs 1C; $p<0.001$, Figs 1E, respectively), while the mortality of the CHE to the CR and the CHE/GDP to the CR do not yield significant results ($p=0.997$, Figs 1D; $p=0.101$, Figs 1F, respectively). In the correlation of MIRs, the results revealed a significant association for the HDI, CHE per capita, USD, and CHE/GDP with the MIR in lip and oral cancer (coefficient correlation: -0.597 , $p<0.001$; coefficient correlation: -0.652 , $p<0.001$; coefficient correlation: -0.651 , $p<0.001$ respectively, Fig 2).

Discussion

In our study, we analyzed and compared the incidence, mortality, HDI and CHE of selected countries. Asia has the most cases and deaths among all regions; these results showed the correlation between the geographic distribution of betel chewing and high oral cancer incidence and mortality. In Asia, especially Southeast Asia, betel quid chewing with different ingredients is a prevalent oral habit [5]. Betel quid has been considered a carcinogen by the International Agency for Research on Cancer (IARC) for years [25]. Previous results showed that betel quid chewing has a significant impact on oral cancer and precancer [26]. A longer duration and greater daily amount of betel quid chewing will also increase the risk of oral cancer [27].

We determined that countries with higher HDIs and CHEs have higher incidence rates (Fig 1). This result supports the findings of a previous study that indicates that cancer incidence burden is greater in countries with higher HDIs [28]. These findings may be due to the tendency of more developed countries to have relatively comprehensive medical facilities, cancer screening systems and patient education.

Some novel methods, such as Toluidine blue staining, brush biopsy, chemiluminescence and tissue fluorescence spectroscopy, aid early diagnosis in the screening of oral cancer [29]. Early detection of oral cancer and public awareness about oral cancer screenings could reduce mortality rates and contribute to better outcomes [30]. Previous results also showed that socioeconomic disparities influence the frequency of oral cancer screening and screening methods [7], which affect the severity at diagnosis and prognosis [31].

However, when corrected incidence and mortality results with MIR, we discovered that more developed countries have lower MIRs (Fig 2), which indicates longer survival rates. A retrospective study showed that advanced preoperative image assessment, efficient radiotherapy and improved operative techniques enabled a substantial increase in the survival rate in recent decades [32]. In addition to operative resection, chemotherapy and radiation therapy, new options such as immunotherapy and target therapy have become increasingly popular in treating oral cancer, especially in advanced stages [8]. Due to the deeper understanding of oncogenic and epigenetic pathways of oral cancer, more biomarkers for identifying invasive and metastatic potential tumors are discovered, and precision therapy based on genetic findings is improving [33]. Thus, countries with higher HDIs and CHEs may facilitate early detection, in combination with effective treatment, and cause higher incidence rates but lower MIRs, which is compatible with our results.

A previous paper showed that the MIR falls short of comprehensive follow up, which would not be able to replace cancer survival rates or prognostic data from long-term follow up or a cohort study [34]. However, other studies showed that the MIR is a simple and efficient method for identifying cancer control [35]. The MIR is also shown to be a suitable method for examining cancer screening and treatment programs worldwide [20].

Limitations

Our results still have some limitations. First, some important risk factors of lip and oral cancer, such as alcohol consumption, smoking, betel chewing, and other oral behaviors among different countries, were not recorded and fully analyzed. These risk factors may have important roles in explaining and determining the incidence and mortality rates among countries and regions. Second, the feasibility of using WHO rankings and e-GDP to represent the healthcare disparities of countries has not been confirmed to specifically apply to different cancers. Other factors, such as national health care systems, disparity in access to cancer care, and insurance coverage, should also be analyzed. Despite these limitations, the MIR appears to provide more accessible data when compared with long-term follow up survival surveys.

Conclusions

The MIR for lip and oral cancer is significantly associated with the HDI, CHE per capita, and CHE/GDP. Countries with higher HDIs, higher CHE per capita, and higher CHE/GDP tend to have longer survival rates.

Abbreviations

MIR: mortality-to-incidence ratio; WHO: the World Health Organization; HDI: human development index; CHE: current health expenditure; GDP: gross domestic product; CR: crude rate; ASR: age standardized rate.

Declarations

Ethics approval and consent to participate: Not Applicable.

Consent for publication: Not Applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are publicly available in Global Cancer Observatory (GLOBOCAN) database (<https://gco.iarc.fr/today/>), United Nations Development Programme/Human Development Report Office (<http://hdr.undp.org/en>) and World Health Statistics database (https://www.who.int/gho/publications/world_health_statistics/en/).

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Lip and oral cavity cancer, ICD-10 C00-06, epidemiological data were obtained from the Global Cancer Observatory (GLOBOCAN) database (<https://gco.iarc.fr/today/>), which is a public access database that provides contemporary estimates of cancer epidemiology for 185 countries in 2018. The HDI was obtained from the United Nations Development Programme, Human Development Report Office (<http://hdr.undp.org/en>). The data on health expenditures, including the per capita current health expenditure (CHE) and ratio of CHE to the percentage of gross domestic product (CHE/GDP), were obtained from the World Health Statistics database (https://www.who.int/gho/publications/world_health_statistics/en/).

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Figures

Figure 1

Association between HDI, CHE and CRs of (A, C, and E) incidence, and (B, D, and F) mortality in lip and oral cancer.

Figure 2

(A) HDI, (B) CHE per capita, and (C) CHE/GDP are significantly associated with the MIR for lip and oral cancer.