Epidemiology of renal cancer in developing countries: Review of the literature

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Abstract

Introduction: Renal cell carcinoma (RCC) is the ninth most common cancer in men, and the 14th most common cancer in women. It has been reported that the incidence of RCC is rising. These changes are more common in developed countries because of better screening programs and disease registry. The aim of this article is to review the epidemiology of RCC around the world.

Methods: A literature review of four databases was performed: PubMed, Embase, Lilacs, and Scielo. Studies of incidence, prevalence, mortality, and survival of RCC were taken from different countries. Studies included were published in the last 10 years. Two reviewers independently selected the studies.

Results: A total of 5275 references were reviewed by title and abstract. In the end, 42 references were selected for full-text review. The global incidence and prevalence of cancer vary. The highest incidence was described in North America and Northern Europe. In Canada, by 2007 the incidence was 17.9/100 000 and 10.3/100 000 in males and females, respectively. Developing countries like Colombia have fewer incidence rates, with less information in poor-income areas.

Conclusions: We have seen a rise in the incidence and mortality of RCC globally. There is an association between RCC and smoking, obesity, hypertension, and socioeconomic status. Seeing the epidemiological data from some regions in developing countries and the lack of specialists in those places, it can be deduced there is underreporting of the disease that reveals the need to improve both surveillance and disease registration programs, especially in these countries.

Introduction

Renal cell carcinoma (RCC) is the ninth most common cancer in men and 14th most common cancer in women.[1] In 2012, 143 000 deaths by RCC were estimated, making it the 16th most common cause of cancer death globally.[1] In recent decades, there has been an increased incidence associated with better diagnosis of the disease and exposure to various risk factors.[2] The highest incidence rates can be found in developed countries, mainly Northern and Eastern Europe, as well as North America.[3]

Unlike other cancers, the incidence of RCC has had a significant rise globally. This is associated with better screening programs and disease registration, factors that have also reduced mortality in countries like France, Germany, and Italy.[4]

Some of the reported risk factors for RCC include gender (more prevalent in men) and age (more prevalent in older adults);[4] however, because of the increased incidence, some studies have identified other associated factors, such as hypertension by chronic use of diuretics, diabetes, urinary tract infections, exposure factors (i.e., smoking, asbestos, radiation), and lifestyle factors (diet and obesity).[5]

In Canada, according to statistics from GLOBOCAN 2012, there have been more than 1000 new cases and 400 more deaths since 2012, and the number of RCC cases estimated by the year 2020 is 4139 in men (with 1373 deaths) and 2565 in women (with 792 deaths).[6]

While Canada counts on the Canadian Cancer Registry, other countries get their epidemiological data from local population bases. Colombia, for example, has the oldest database in Latin America, with the population registry of cancer in Cali (RPCC) containing information dating back to 1962.[7] However, because of the geographic and sociocultural difference in the country, RPCC information is insufficient to calculate the national epidemiological data,[8] a scenario that can be seen in many other developping countries.

Given the lack of accurate and recent epidemiological data on RCC in many parts of the world, we sought to perform a literature search to determine the incidence, prevalence, and mortality of this disease globally.

Methods

A review of the literature was performed in four different databases (PubMed, Embase, Lilacs, and Scielo) on any information concerning the field of epidemiology in renal cancer.

The search criteria were established in the form of free text and indexed terms. To characterize the RCC, we used the free terms: "kidney cancer," "renal cancer," "kidney neoplas*," and "renal neoplas*." For epidemiological studies, the terms in free text were: "incidence," "prevalence," "epidemiology." "mortality," and "burden of disease," "cost of illness;" indexed terms included "incidence" and "prevalence." The search was limited to publications in the last 10 years. A grey literature search was also performed on the pages of The National Technical Information Service (NTIS) and the European Association for Grey Literature Exploitation (EAGLE), however, no additional relevant information was found.

The articles were all original studies that provided epidemiological information on incidence, prevalence, mortality, survival, and disease burden of RCC. Studies that described their information in specific subgroups (specific histological type or ethnic group) were excluded. References were reviewed by title and abstract by two independent reviewers. From the first selection of articles, references were reviewed in full text, ensuring they provided previously mentioned information of interest on RCC. Duplicate studies were removed and studies written in any language other than English or Spanish were ignored.

Results

The search yielded a total of 5275 references that were reviewed by title and abstract. In seeking local references, four studies from non-indexed journals were included. Three hundred thirty-eight references were selected for full text review, of which 300 were excluded because they did not include the epidemiological data of interest. References for which full text was not available (poster format or abstract) were excluded, as were those in languages other than English or Spanish. Forty-two articles were analyzed for data extraction (Fig. 1).

All studies were observational; most of them were cross-sectional studies that drew their information from the databases of each country. One of the limitations of this review lies in the methodology of most of the studies, as disease registration programs have different quality levels and coverage in each country, preventing a proper comparison of the results.[9] Yang et al refer to a possible under-reporting of disease,[10] and in their study, Villanueva et al discuss the need to improve epidemiological surveillance programs.[11]

Among the included studies, two were global studies, 14 assessed populations from Europe, 14 from America (of which eight corresponded to Latin American literature), eight from Asia and Oceania, and four from Africa and the Middle East.

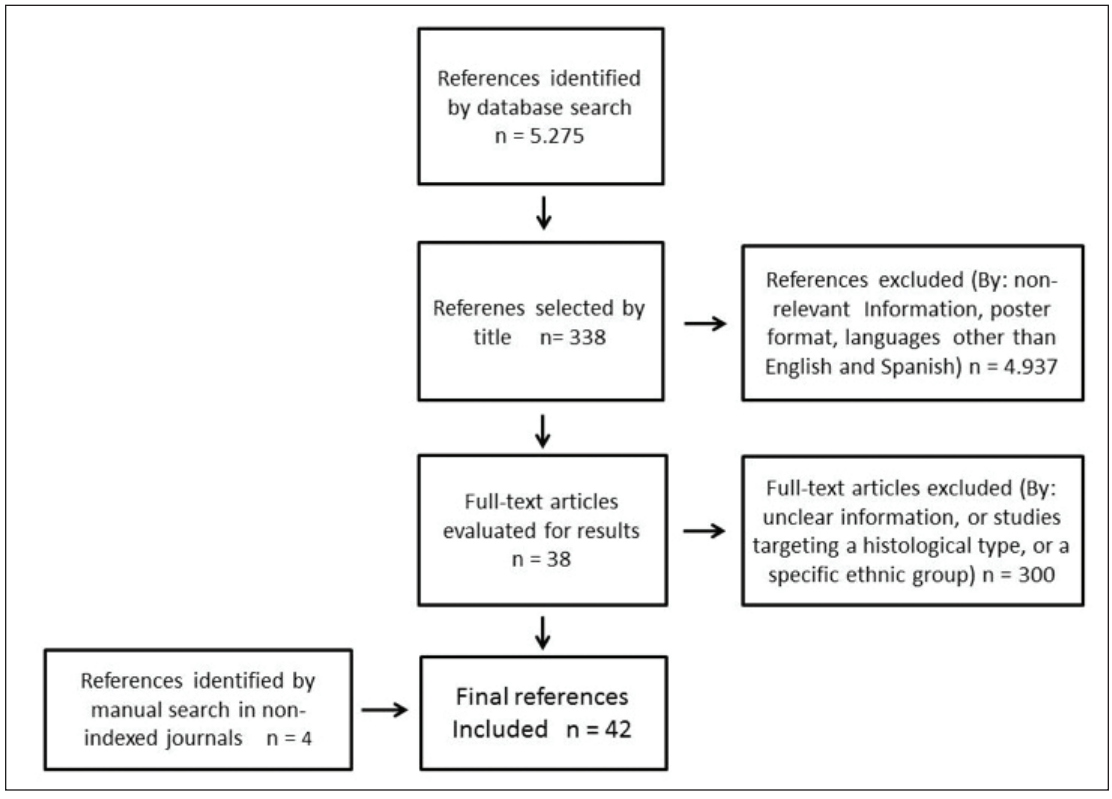

Fig. 1. Flow chart of the search.

Global data

Patel et al found that the highest incidence of RCC was in North America (11.8/100 000 general population).[3] Znaor et al described the incidence and mortality rates between 2003 and 2007; the highest was found in Europe, specifically the Czech Republic, the lowest in Asia, mainly Thailand and Korea.[1] Patel et al referred to the characteristics of each population (genetics and exposure to risk factors), as well as socioeconomic levels as possible explanations for the epidemiological differences between countries, finding higher incidences in developed countries and an increased mortality in developing countries.[3] Znaor et al also concluded an overall increase in the incidence of RCC due to the development of better diagnostic techniques[1] (Table 1).

European data

Four studies evaluated multiple countries in Europe. One such study by Ljungberg et al found a gender difference in incidence (15.8/100 000 in men and 7.1/100 000 in women). The study also concluded that both incidence and mortality have been declining due to the reduced cigarette consumption in these populations and better occupational hygiene.[4]

The remaining studies were conducted in Germany, Holland, Italy, England, Scotland, Ireland, Denmark, and Spain for a total of 10 studies. The highest incidences were found in Germany and Holland, with the latter having rates of 16.9/100 000 in men and 9.2/100 000 in women.[12,13] The lowest incidence was seen in Spain, with 8.2/100 000 in men and 3.7/100 000 in women between 2003–2007,[14] with a tendency toward increasing rates.[15] Ireland also has an increasing tendency; Falebita et al associated this finding with better diagnosis and registration.[16] A study by Wihlborg et al based in Denmark described a change in incidence over time, rising from 3.95/100 000 in the time period from 1944–1948 to 7.30/100 000 from 1969–1973, and decreasing to 7.01/100 000 from 1999–2003. Authors explained the first increase by improvements made in diagnosis, while the decreased incidence in more recent years was attributed to a decrease in cigarette consumption.[17] A study by Maruthappu et al in England found differences in incidence by ethnicity.[18]

Mortality was assessed in eight studies, three with information from multiple countries. The highest mortality was found in the Czech Republic (9/100 000 in men and 3.7/100 000 in women), the lowest in Greece, Portugal, and Luxembourg.[19] Most studies agreed that mortality is decreasing and this is associated with more timely diagnosis, better treatments, and less tobacco consumption.[2,4,19]

The other five studies were conducted in Holland, Ireland, Italy, and two in Spain. The highest mortality was found in Holland (7.3/100 000 in men and 3.8/100 000 in women),[13] the lowest in Italy (2.39/100 000 in men and 1.61/100 000 in women).[20] Although some studies described a decrease in mortality, others, such as Opeyemi et al in Ireland, showed an increase in mortality in recent decades.[16]

Five-year survival was evaluated in four articles; one was conducted in multiple countries. The study by Mark-Gragera et al found differences by region, with the rate being greatest in Central Europe (64.6 %) and lowest in Northern Europe (55.8%). The difference was attributed to the difference in diagnosis and intervention programs in each region.[9] The other four studies were conducted in Ireland, Denmark, and Scotland, the latter having the lowest survival (39–42 %).[21] Factors related to higher five-year survival rates included better diagnosis and intervention, as well as higher socioeconomic and educational level.[22]

Asia and Oceania

Eight studies were found from Japan, China, Korea, and Australia. Japan had the highest incidence rates for RCC, with Marugame et al showing an incidence of 11.6/100 000 in men and 5.6/100 000 in women.[23] Marumo et al also showed an increased incidence in Japan, and indicated a need to study its relationship with known risk factors.[24] Zheng et al discussed how the prevalence of cancer is higher in urban areas compared to rural ones and how this is associated with increased life expectancy.[25]

In Korea, the incidence was slightly lower than in Japan; Jung et al described a mortality rate in men of 2.3/100 000 and 0.9/100 000 in women, with a five-year survival of 77.7 %.[26,27]

Studies from Australia show an increase in both the incidence of RCC and the survival rate in the last five years.[28,29]

Africa and Middle East

Four studies were found from Saudi Arabia, Pakistan, Morocco, and Iran. The lowest incidence of RCC was found in Pakistan (1.4/100 000).[30] The other studies showed an increased incidence in recent years.[31-33] Mirzaei et al associated the increase with better recording of the disease and an increased exposure to risk factors.[32]

America

In America, 14 articles were found: six from North America and eight from Latin America. The study by Pinheiro et al conducted in the U.S. found similar incidence rates among different ethnic groups, with slightly higher rates in Caucasian (18/100 000 in men, 8.7/100 000 in women), followed by the Hispanic (17.3/100 000 in men, 7.7/100 000 in women) and black populations (14.7/100 000 in men, 7.2/100 000 in women).[34] Some studies showed increasing incidence rate over several years. Gandaglia et al, for

Table 1. Main outcomes of the search

Author	Year	Journal	Outcome measure	Results	Geographic zone
Global					
Patel et al[3]	2012	*J Urol*	Incidence	North America 11.8/100 000 Australia 8.3/100 000 Europe 8.1/100 000 Africa 1.2/100 000 Asia 1/100 000	Global
Znaor et al[1]	2015	*Eur Urol*	Incidence	Highest incidence was found in Czech Republic (9.9/100 000), lowest in Thailand (0.8/100 000)	Global
			Mortality	Highest mortality was found in Czech Republic (3.6/100 000), lowest in Korea (0.6/100 000)	
Europe					
Marcos-Gragera et al[9]	2015	*Eur J Cancer*	Survival	North Europe 55.8% to 5 years Central Europe 64.6% to 5 years South Europe 64.4% to 5 years East Europe 57.5% to 5 years	Europe
Levi et al[2]	2008	*BJU Int*	Mortality	1990–1994 Males of 4.75/100 000 1990–1994 Females of 2.12/100 000 2000–2004 Males of 4.13/100.000 2000–2004 Females of 1.76/100 000	Europe
Bosetti et al[19]	2011	*Eur Assoc Urol*	Mortality	1994: 4.9/100 000 2006: 4.3/100 000 Highest incidence in Czech Republic males (9/100 000); females (3.7/100 000), lowest in Greece and Portugal	Europe
Ljungberg et al[4]	2011	*Eur Urol*	Incidence	Males 15.8/100 000 Females 7.1/100 000	Europe
			Mortality	Males 6.5/100 000 Females 2.7/100 000	
Stang et al[12]	2014	*Emerg Themes Epidemiol*	Incidence	Males 15.7/100 000 Females 7.6/100 000	Germany
van de Schans et al[13]	2012	*Eur J Cancer*	Incidence	Males 16.9/100 000 Females 9.2/100 000	Holland
			Mortality	Males 7.3/100 000 Females 3.8/100 000	
Eriksen et al[22]	2008	*Eur J Cancer*	Incidence	Males 15/100 000 Females 8/100 000	Denmark
			Survival	Males 39% to 5 years Females 44% to 5 years	
Wihlborg et al[17]	2009	*Urology*	Incidence	1944–1948: Males 3.95/100 000 1944–1948: Females 2.72/100 000 1969–1973: Males 7.30/100 000 1969–1973: Females 4.77/100 000 1999–2003: Males 7.01/100 000 1999–2003: Females 3.6/100 000	Denmark
Maruthappu et al[18]	2015	*BMC Cancer*	Incidence	Caucasian 5.9/100 000; Black 5.5/100.000	England
Falebita et al[16]	2009	*Int Urol Nephrol*	Incidence	1994: Males 7.1/100 000 1994: Females 3.3/100 000 2005: Males 8.0/100 000 2005: Females 5.7/100 000	Ireland
			Mortality	1994: 3.6/100000 2004: 4.7/100 000	
			Survival	1994–1996: 69.4% to 5 years 2000–2002: 69.5 % to 5 years	

Table 1 (cont'd). Main outcomes of the search

Author	Year	Journal	Outcome measure	Results	Geographic zone
Europe (cont'd)					
Falebita et al[16]	2009	*Int Urol Nephrol*	Incidence	1994: Males 7.1/100 000 1994: Females 3.3/100 000 2005: Males 8.0/100 000 2005: Females 5.7/100 000	Ireland
			Mortality	1994: 3.6/100000 2004: 4.7/100 000	
			Survival	1994–1996: 69.4% to 5 years 2000–2002: 69.5 % to 5 years	
Westlake et al[21]	2008	*Br J Cancer*	Survival	Between 39% and 42% to 5 years	Scotland
Souza et al[15]	2011	*Actas Urológicas Españolas*	Prevalence	2002: Males 53.65/100 000 2002: Females 23.04/100 000 2012: Males 57.1/100 000 2012: Females 44.08/100 000 2022: Males 59.57/100 000 2022: Females 81.37/100 000	Spain
			Incidence	2002: Males 8.79/100 000 2002: Females 4.92/100 000 2012: Males 9.17/100 000 2012: Females 8.97/100 000 2022: Males 9.55/100 000 2022: Females 16.4/100 000	
			Mortality	2002: Males 4.19/100 000 2002: Females 1.97/100 000 2012: Males 4.38/100 000 2012: Females 3.59/100 000 2022: Males 4.56/100 000 2022: Females 6.56/100 000	
Clèries et al[14]	2013	*Clin Transl Oncol*	Mortality	Males 2.3/100 000 Females 0.8/100 000	Spain
			Incidence	Males 8.2/100 000 Females 3.7/100 000	
Arfè et al[20]	2011	*Eur J Cancer Prevent*	Mortality	Males 2.39/100 000 Females 1.61/100 000	Italy
Asia & Oceania					
Marumo et al[24]	2007	*Int J Urol*	Incidence	Males 8.2/100 000 Females 3.6/100 000	Japan
Marugame et al[23]	2006	*Jap J Clin Oncol*	Incidence	Males 11.6/100 000 Females 5.6/100 000	Japan
Yang et al[10]	2013	*PLOS ONE*	Incidence	Males 5.64/100 000 Females 3.33/100 000	China
Zheng et al[25]	2015	*Cancer Letters*	Prevalence	Prevalence to 5 years for 2011: Males 17.9/100 000 Females 10.4/100 000	China
Jung et al[26]	2013	*Kor Cancer Assoc*	Incidence	Males 10.1/100 000 Females 4.3/100 000	Korea
			Mortality	Males 2.3/100 000 Females 0.9/100 000	
			Survival	77.7% to 5 years	
Yi et al[27]	2013	*J Prevent Medicine Public Health*	Incidence	9.7/100 000	Korea

Table 1 (cont'd). Main outcomes of the search

Author	Year	Journal	Outcome measure	Results	Geographic zone
Asia & Oceania (cont'd)					
Luke et al[28]	2011	*Asian Pacific J Cancer*	Incidence	1980–1984: 6.29/100 000 2005–2008: 12.46/100 000	Australia
			Mortality	1980–1984: 3.39/100 000 2005–2008: 4.24/100 000	
			Survival	61.7% to 5 years	
Australian Institute of Health and Welfare[29]	2013	*Asia Pacific J Clin Oncol*	Survival	1982–1987: 4% to 5 years 2006–2010: 72% to 5 years	Australia
Africa & Middle East					
Abomelha et al[31]	2011	*Arab J Urol*	Incidence	2.4/100 000	Arabia Saudí
Mirzaei et al[32]	2015	*Asian Pacific J Cancer Prevent*	Incidence	2003: Males 1.39/100 000 2003: Females 0.96/100 000 2009: Males 2.99/100 000 2009: Females 2.05/100 000	Iran
Badar et al[30]	2016	*BMJ Open*	Incidence	2010: 1.5/100 000 2012: 1.4/100 000	Pakistan
Tazi et al[33]	2013	*E Cancer*	Incidence	Males 2.3/100 000 Females 1.7/100 000	Morroco
America					
Chatenoudet al[40]	2014	*Annals Oncol*	Mortality in males	Uruguay 5.97/100 000 Argentina 4.85/100 000 Chile 4.2/100 000 Brazil 1.71/100 000 Colombia 1.25/100 000 Ecuador 1.17/100 000	Latin America
			Mortality in females	Uruguay 2.32/100 000 Chile 1.88/100 000 Argentina 1.68/100 000 Colombia 0.79/100 000 Ecuador 0.76/100 000	
Pinherio et al[34]	2009	*Cancer Epidemiol Biomarkers Prev*	Incidence	Males – Hispanic 17.3/100 000 Males – Caucasian 18/100 000 Males – Black 14.7/100 000 Females – Hispanic 7.7/100 000 Females – White 8.7/100 000 Females – Black 7.2/100 000	USA
Lang et al[37]	2007	*Urol Oncol*	Burden of disease	Annual cost for RCC up to 2005 was $4.4 billon USD, with a cost per patient of $40.176: 92.4% costs for medicines and procedures, 7.6% for disability	USA
Kamel et al[39]	2012	*J Urol*	Burden of disease	1972–1976 343.912 PYLL 2002–2006 479.355 PYLL	USA
Li et al[38]	2010	*Urology*	Burden of disease	PYLL Caucasian 104 126 (50.59 %) PYLL Black 112 438 (62.10 %) PYLL Hispanic 10 010 (72.81 %) PYLL General 129.216 (52.94 %)	USA
Gandaglia et al[35]	2014	*Can Urol Assoc J*	Incidence	1975: 2.99/100 000 2009: 12.16/100 000	USA
			Mortality	1975: 2.24/100 000 2009: 5/100 000	
			Survival	1975: 47.5% to 5 years 2005: 64.9% to 5 years	

Table 1 (cont'd). Main outcomes of the search

Author	Year	Journal	Outcome measure	Results	Geographic zone
America (cont'd)					
Otterstatter et al[36]	2014	*Cancer Causes Control*	Incidence	1986: Males of 13.4/100 000 1986: Females of 7.7/100 000 2007: Males of 17.9/100 000 2007: Females of 10.3/100 000	Canada
			Mortality	2025 male mortality will be 17.9/100 000; 2025 female mortality will be 8.7/100 000	
			Survival	68% to 5 years	
Montes et al[41]	2004	*Revista Chilena de Urología*	Incidence	General 6.95/100 000 Males 9.67/100 000 Females 4.14/100 000	Chile
Villanueva et al[11]	2014	*Gaceta Médica de México*	Incidence	2.5/100 000	Mexico
Bosetti et al[42]	2011	*Eur J Cancer Prevent*	Mortality	1999: Males 2.2/100 000 1999: Females 2.35/100 000 2007: Males 2.35/100 000 2007: Females 1.34/100 000	Mexico
Guarnizo et al[44]	2012	*Colombia Médica*	Incidence	Males 3.4/100.000 Females 2.4/100 000	Colombia
Uribe et al[45]	2012	*Colombia Médica*	Incidence	Males 2.4/100 00 Females 1.3/100 000	Colombia
Yépez et al[46]	2012	*Colombia Médica*	Incidence	1998–2002: Males 2.1/100 000 1998–2002: Females 1.1/100 000 2003–2007: Males 1.7/100 000 2003–2007: Females 1.4/100 000	Colombia
Pardo et al[43]	2015	*Instituto Nacional de Cancerología*	Incidence	Males 2.7/100 000 Females 1.9/100 000	Colombia
			Mortality	Males 1.1/100 000 Females 0.7/100 000	
			Survival	Absolute survival of 51.9 % to 5 years	

PYLL: potential years of life loss; RCC: renal cell carcinoma.

example, described an incidence of 2.99/100 000 in 1975 compared to 12.16/100 000 in 2009. This increase was associated with improvements in diagnostic techniques and an aging population; however, they suggested the need to investigate a possible increase in risk factors as well.[35] In Canada, Otterstatter et al showed similar results, finding an increasing RCC incidence associated with increased risk factors, such obesity and hypertension.[36] In terms of mortality, the study by Gandaglia et al in the U.S. found a tendency toward increasing rates in recent years (2.24/100 000 in 1975 to 5/100 000 in 2009),[35] while the Otterstatter study estimated that the mortality attributable to RCC in Canada would reach 17.9/100 000 in men and 8.7/100 000 in women by 2025.[36]

With regard to burden of disease, a U.S. study found the total cost of RCC to be $4.4 billion USD in 2005, which meant an average $40.176 per patient.[37] Li et al showed the potential years of life loss (PYLL) for the Caucasian American population as 129 216 in 2004.[38] Kamel et al found that the PYLL has been increasing in recent decades, which has made RCC a disease that should be particularly worrisome for urologists and the healthcare system globally.[39]

Eight studies were found in the Latin American literature. Chatenoud et al evaluated multiple countries in the region; they found the highest mortality in Uruguay (5.97/100 000 in men and 2.32/100 000 in women) and the lowest in Ecuador (1.17/100000 in men and 0.76/100 000 in women).[40] The other studies were made mainly from Colombia, Mexico, and Chile. Of these, the highest RCC incidence was found in Chile (6.95/100.000 general population).[41] Villanueva et al found an overall RCC incidence in Mexico of 2.5/100 000,[11] with mortality remaining relatively stable over the last several years (2.3/100 000 in men and 1.34/100.000 in women in 1999 and 2.35/100 000 in men and 1.34/100 000 in women in 2007).[42]

In Colombia, Pardo et al found a RCC incidence of 27/100 000 in men and 1.9/100 000 in women. The highest rates were found in Risaralda and Quindío, and the lowest in Chocó and Amazonas. Mortality was found to be 1.1/100 000 in men and 0.7/100 000 in women, and five-year survival was 51.9%.[43] Between 2003 and 2007, Manizales was

the city with the highest incidence (3.4/100 000 in men and 2.4/100 000 in women), followed by Bucaramanga (2.4/100 000 in men and 1.3/100 000 in women), and Pasto (1.7/100 000 in men and 1.4/100 000 in women).[44-46]

Discussion

A global difference in RCC incidence, mortality, and survival rates can be observed. The highest incidence was found in Europe, mainly in the Czech Republic and Denmark, followed by North America, Australia, South America, and Asia. Mortality rates also followed this pattern, with higher rates found in Europe and the lowest ones in Asia.

In every country, the tendency is towards increasing incidence; however, some studies, such as the ones by Ljungberg et al and Clèries et al, note a stabilization of incidence in recent years. This result is attributed to good disease registration programs and better control of risk factors.[4,14]

In terms of mortality rates, studies by Levi et al and Bosetti et al show a decrease over recent years.[2,19] Despite these findings, we can't confirm that these trends are shared in all regions, given the difference in diagnostic technologies and the reliability of disease registration programs throughout the world. Furthermore, under-reporting of disease is a limiting factor, as pointed out by Yang et al and Wojcieszak et al,[10,47]as this can make it difficult to compare data between countries.

Of particular interest to us are studies that found a relationship between incidence/mortality rates and socioeconomic status. Some studies reported both a lower incidence and lower five-year survival in developing countries with fewer resources.[3,22,48] These results may be associated with greater difficulties in access to healthcare services and the lack of a urological specialty in some areas.[49]

Although several studies identified greater exposure to risk factors, such as smoke, diet, obesity, and hypertension, as potential elements associated with epidemiological differences in RCC rates, more in-depth research is needed on these factors and their role in the development of RCC.

Another interesting fact is that almost all the studies in our analysis found a difference in incidence by gender and/or race, with higher incidences and mortality rates reported in men and Caucasian populations.

Given the increasing incidence of RCC, there is a global need to improve public health policies aimed at promoting early diagnosis, creating comprehensive national registries, and implementing earlier treatment plans so as to improve outcomes for patients with RCC.

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This paper has been peer-reviewed.

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