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Trend in gastric cancer mortality rate in Peru: Segmented regression model 1995 - 2013

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GASTRIC CANCER MORTALITY RATE TREND IN PERU: SEGMENTED REGRESSION MODEL FROM 1995 TO 2013

TENDENCIA DE LA TASA DE MORTALIDAD POR CÁNCER GÁSTRICO EN PERÚ: MODELO DE REGRESIÓN SEGMENTADA DE 1995 A 2013

Diego Venegas-Ojeda[1,a], Ysela Dominga Agüero-Palacios[2,b]

ABSTRACT

Objective: To analyze the gastric cancer mortality trends in Peru from 1995 to 2013 and their differences by sex, age groups, political and geographic regions. **Methods:** Ecological time-series study based on 49,690 death records from the Ministry of Health, from 1995 to 2013; Crude, specific and standardized mortality rates (SMR) were calculated by year; according to sex; age group; political and geographic regions, to analyze trends by estimating joinpoints and annual percentage changes (APC); through segmented regression models using the Joinpoint Regression Desktop software version 4.5.0.0. **Results:** The SMR trend due to gastric cancer in Peru was decreasing, falling from 16.1 x 100 000 inhabitants. in 1995 to 11.4 x 100 000 inhabitants. in 2013 (CPA: -2.3), observing decreasing trends in 17 of 25 political regions. Differences were found: faster decrease in women (CPA -2.5) versus men (-2.0) and at older age (CPA for 75 - 79 years: -2.57 versus CPA for 40 - 44: -1.39); Three geographical areas with high mortality were identified: central Andes, northern area and central coast, there are growing trends in Huancavelica, Ayacucho and Pasco. On the Coast, mortality has decreased since 1998; in the Sierra and Selva it decreases significantly as of 2009. **Conclusions:** The trend of SMR due to gastric cancer was decreasing for the period 1995 - 2013 with disparities by sex, age groups, political and geographic regions.

Key words: Trends; Mortality rate; Regression analysis; Gastric cancer; Peru (source: MeSH NLM).

RESUMEN

Objetivo: Analizar las tendencias de mortalidad por cáncer gástrico en Perú de 1995 a 2013 y sus diferencias por sexo, grupos etarios, regiones políticas y geográficas. **Métodos:** Estudio ecológico de series de tiempo basado en 49 690 registros de defunción del Ministerio de Salud, de 1995 a 2013; se calcularon tasas de mortalidad brutas, específicas y estandarizadas por año; según sexo, grupo de edad, regiones política y geográfica, para analizar tendencias estimando joinpoints y cambios de porcentaje anual (CPA) mediante modelos de regresión segmentada utilizando el software Joinpoint Regression Desktop versión 4.5.0.0. **Resultados:** La tendencia de la tasa de mortalidad estandarizada (TME) por cáncer gástrico en Perú fue decreciente (16,1 x 100 000 hab. en 1995 a 11.4 x 100 000 hab. en 2013) (CPA: -2,3), observándose tendencias decrecientes en 17 de 25 regiones políticas. Se encontraron diferencias: decremento más acelerado en mujeres (CPA -2,5) versus hombres (-2,0) y a mayor edad (CPA para 75 - 79 años: -2,57 versus CPA para 40 – 44: -1,39); destacan tres regiones con elevada mortalidad: Andes centrales, zona norte y costa central; existen tendencias crecientes en Huancavelica, Ayacucho y Pasco. En la Costa la mortalidad decrece desde 1998; en la Sierra y Selva decrece significativamente a partir del 2009. **Conclusiones:** La tendencia de la TME por cáncer gástrico fue decreciente para el período de 1995 – 2013 con disparidades por sexo, grupos etarios, regiones políticas y geográficas.

Palabras clave: Tendencias; Tasa de mortalidad; Modelo de regresión segmentada; Análisis de regresión; Cáncer gástrico; Perú (fuente: DeCS BIREME).

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INTRODUCTION

Worldwide, the incidence and mortality of gastric cancer have been drastically reduced in the last 70 years [1,2,3]. Despite this, it is the fifth most common cancer and the third leading cause of death due to cancer. According to the International Agency for Research on Cancer (IARC), there were 1,033,701 new cases of gastric cancer (incidence rate 11.1 per 100,000 inhabitants) and 782,685 deaths from this disease (mortality rate of 8, 2 per 100,000 pop) in 2018[4,5]. About 3 out of 4 new cases and deaths from gastric cancer occur in developing countries[6].

In Peru, cancer ranks second in mortality since the 1990s[7]. The incidence of gastric cancer is 16.1 per 100,000 inhabitants, one of the highest in the world, surpassed by Asian countries such as South Korea (39.6), Mongolia (33.1), Japan (27.5), China (20.7), Bhutan (19.4) Kyrgyzstan (18.6) and other countries such as Chile (17,8) and Belarus (16.5)[4]. Furthermore, the incidence rate is similar to the mortality rate in Peru due to patients' poor survival after they are diagnosed[8].

Regional variations reflect differences in eating habits, food storage, and availability of fresh produce, as well as the prevalence of Helicobacter pylori infection[9,10]. Chronic H. pylori infection is the strongest identified risk factor for stomach cancer[11].

Some publications descriptively show a decreasing trend in gastric cancer mortality in Peru, although in a shorter period, such as 10 years (2005 to 2014)[12] and 8 years (2008 to 2015)[13], showing a reduction in the standardized rate. There are differences within Peru for gastric cancer mortality. The highest rates are found in the central highlands and the coast. The political regions with the highest mortality rate are Huánuco, Huancavelica, and Junín[14], which are also regions with higher poverty indicators, less access to health services, less availability of drinking water[15]. In rural areas, the population drains its waste into the local river. This water is usually the same one treated for human consumption, finding a low concentration of chlorine. All of these factors favor the spread of H. pylori infection[8]. Although it is also followed by more urbanized regions such as La Libertad and Callao[12].

Cancer is a disease of high cost and social impact on the population and implies a greater deployment of economic, human, and technological resources that must be optimally provided by health managers. Thus far, the reports of trends in mortality rates have been descriptive. They have used non-parametric trend analysis or linear log models. Therefore, the importance of improving epidemiological knowledge when performing the analysis of trends under a segmented regression model over long periods (19 years). In this way, when estimating change points or joinpoints, the influence of variables that change over time can be hypothesized, either by a planned intervention or unintentional phenomena that alter the environment[16,17].

This research aimed to analyze the trends in gastric cancer mortality in Peru applying segmented regression models, during the period 1995 - 2013 and their differences by age groups, gender, political region, and geographic region.

METHODS

Type of study

An ecological time series study was carried out based on standardized mortality rates from stomach cancer.

Population and sample

The population was the set of all the executions of the stochastic process (ensemble) constituted by the standardized annual death rates for gastric cancer in Peru, from 1995 to 2013, the unit of analysis was the population of the country in each period. The sample consisted of the standardized annual death rates for the mentioned period.

Ethical aspects

The data used for this research are from a secondary source and were provided anonymously by the General Office of Statistics and Informatics of the Ministry of Health[18].

Data collection and processing

Records with a underlying cause of death coded according to the International Classification of Diseases (ICD) were selected, using the C152 code ninth version (ICD-9) from 1995 to 1999 and the C16 code of the tenth edition (ICD-10), from the year 2000 onwards. 97.9% of the records were filled out by health professionals.

The annual country population was obtained from the census projections of the National Institute of Statistics and Informatics[19]. The gross and specific rates expressed per 100,000 inhabitants were calculated with this data by gender, five-year age groups (except those under 40 and 80 and over), and geographic and political regions. The population estimated by the World Health Organization (WHO)

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was used as the reference population to calculate the age-standardized rates[20].

Análisis estadístico

The temporal trend of the standardized mortality rates was analyzed using a segmented regression model, gender, age, political regions of origin (departments), and geographic (coast, mountains and jungle) were incorporated as independent variables, by considering the belonging of the majority of the population of a political region to a certain geographic area.

A joinpoint segmented regression model was fitted in order to identify the periods between the years 1995 and 2013 in which there were significant changes in the standardized mortality rate.

$$E\left(\frac{y_i}{x_i}\right) = \beta_0 + \beta_1 x_i + \gamma_1 (x_i - \tau_1)^+ + \cdots + \gamma_n (x_i - \tau_n)^+ + \quad ; i = 1,2,\ldots,n. \qquad (1)$$

Where: $(x_i - \tau_k)^+ = \{(x_{i-}\tau_{k)}\ si\ (x_{i-}\tau_{k)} > 0\ 0$ otherwise;

$\beta_0, \beta_1, \gamma_i, \ldots, \gamma_n$ are the regression coefficients and $\tau_{k,}\ for\ k = 1,2,\ldots,m;\ m < n,$ *is the k-th joinpoint* unknown.

The model was adjusted under the hypothesis of the existence of a linear evolution of the natural logarithm of the expected standardized mortality rates and unrelated errors.

The method was selected "Grid search," considering between 0 and 3 joinpoints to locate the joinpoints. As a summary measure, the annual percentage change (CPA, for its initials in Spanish) and the Average Annual Percentage Change (CPAP, for its initials in Spanish) were used. Unlike other trend studies conducted in Peru[12,13], this model made it possible to identify the moment in which significant changes occur in the observed trend.

The evaluation of the goodness of fit of the model and the significance of the changes in the trend was carried out by using the classic Bayesian Information Criterion (BIC) and the parametric Student's t-test for a significance level of 5%.

To adjust the model, the Joinpoint Desktop Software v.4.5.0.0 (Division of Cancer Control and Population Sciences, National Cancer Institute) was used[21].

A map was prepared from the standardized mortality rates (SMD) due to gastric cancer in Peru for 2013 with the rates estimated using the adjusted segmented regression model and they were ordered from highest to lowest in 4 groups, taking as reference the national standardized mortality rate (MNR) of 11.9 per 100,000 pop.

- Very high: when the TME> 150% TMEN,
- High: when the TME: 100 - 150% TMEN,
- Medium: when the TME: 50-100% TMEN,
- Low: when the TME <50% TMEN.

The map prepared from the TMEN softens the standardized mortality rates and allows better identification of vulnerable territories.

RESULTS

A total of 49,690 death records with basic cause of death from gastric cancer were analyzed in Peru from 1995 to 2013. In 1995, the standardized mortality rate was 16.1 per 100,000 inhabitants. In 2013 it decreased to 11.4 per 100,000 inhabitants, observing a statistically significant decreasing trend ($p < 0.05$) and without change points or joinpoints, with a reduction of 2.3% per year (see Table 1).

Table 1. Trends in age-standardized mortality rate due to gastric cancer by gender in Peru from 1995 to 2013. Segmented regression analysis.

Group	TMEE (per 100,000 inhab.)		CPA	CPA	Trend		Period
	Initial	Final		95% CI	t-test	p-value	
Men	18.22	20.79	6.8	[-8.4; 24.6]	1	0.355	1995-1997
	20.79	14.82	-5.1*	[-8.1; -1.9]	-3.7	0.002	1997-2003
	14.82	16.25	0.2	[-2.1; 2.5]	0.2	0.851	2003-2010
	16.25	13.25	-6.2	[-12.2; 0.3]	-2.2	0.1	2010-2013
Women	0.41	0.32	-2.5*	[-3.1;-1.9]	-8.3	< 0.001	1995-2013
Total	16.09	11.41	-2.3*	[-2.8; -1.8]	-8.9	< 0.001	1995-2013

TMEE, for its initials in Spanish: Age-standardized mortality rate, estimated in the model
CPA: Annual percentage change
* Statistically significant trend

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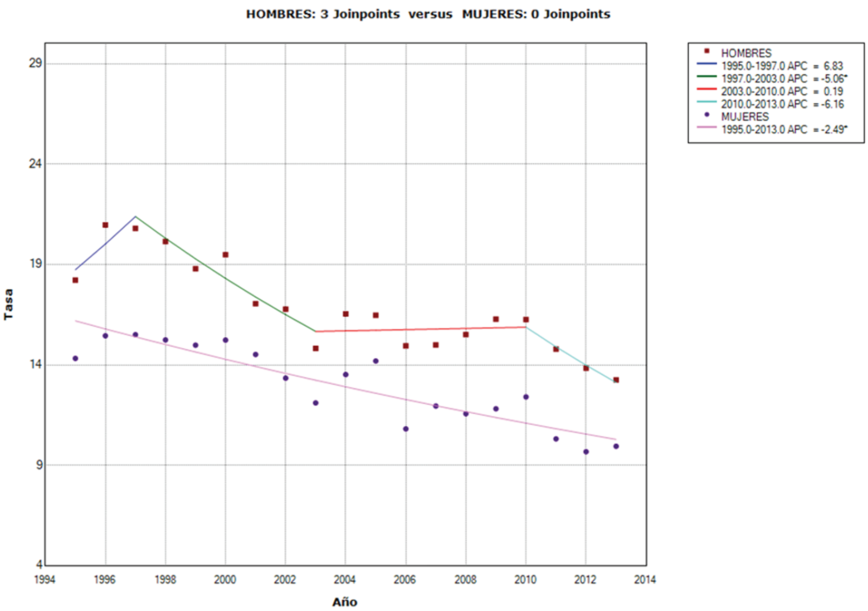
Mortality trends standardized by gender

In men the standardized mortality trend was changing: the optimal segmented regression model showed three joinpoints (BIC: 1,72) which occur in: $(x_i\text{-}t_k)^+=3$; $t_1=1997$, $t_2=2003$ y $t_3=2010$; and determine 4 segments: a) period 1995-1997: increasing trend (CPA 6.8%), not statistically significant b) period 1997-2003, decreasing trend (CPA -5.1%), statistically significant (p value <0 , 05), c) period 2003-2010, slightly increasing trend (CPA 0.2%) and not statistically significant and d) period 2010-2013, decreasing trend (CPA -6.2%), but not statistically significant (see Table 1 , Figure 1).



$$\textit{Hombres}: \; {}^{y_i}/_{x_i} = -128.9 + 0.07x_i - 0.12(x_i - 1997)^+ + 0.05(x_i - 2003)^+ - 0.07(x_i - 2010)^+ \; ; \; i = 1995, \ldots, 2013$$

$$\textit{Mujeres}: \; {}^{y_i}/_{x_i} = 53.04 - 0.03x_i \; ; \; i = 1995, \ldots, 2013$$

Graphic 1. Comparative gastric cancer mortality trend by gender in Peru 1995-2013, segmented regression models.

The optimal segmented regression model for the standardized mortality trend in women was decreasing and statistically significant, with a decrease of 2.5% per year, and does not contain joinpoints (BIC = 2.05). There is no parallelism between men and women (p-value = 0.05). (see Figure 1).

Standardized mortality trends by age group

statistically significant decreasing trend observed, three joinpoints are detected: for the group of 60 to 64 years in the years 1997, 2007 and 2010 and another three; for the 65 to 69 age group in the years 1997, 2003 and 2009. It is observed that the CPA decreases as the age group increases. For example, for the 40-44-year-old group, it was -1.39% annually, while for the 75-79-year-old age group, it was -2.57% annually (see Table 2).

Table 2. Trends in TMEE due to gastric cancer by age group in Peru 1995 - 2013. Segmented regression analysis.

Age group tmee	TMEE (per 100,000 inhab.)		CPA	CPA	Period
	Initial	Final		IC 95%	
< 40 years	0.61	0.42	-2.07*	[-3.1 -1.0]	1995-2013
40 - 44 years	0.41	0.32	-1.39*	[-2.3-0.4]	1995-2013
45 - 49 years	0.62	0.43	-2.00*	[-2.9-1.1]	1995-2013
50 - 54 years	0.94	0.65	-2.06*	[-3.0-1.1]	1995-2013
55 - 59 years	1.22	0.82	-2.19*	[-2.8-1.6]	1995-2013
60 - 64 years	1.47	1.71	8.9	[-17.2-43.2]	1995-1997
	1.71	1.15	-3.7*	[-6.0-1.4]	1997-2007
	1.15	1.41	5.1	[-18.5-35.6]	2007-2010
	1.41	0.89	-13.1*	[-24.1-0.4]	2010-2013
65 - 69 years	1.88	2.45	13.98	[1.3- 0.2]	1995-1997
	2.45	1.52	-7.60*	[-3.6-0.0]	1997-2003
	1.52	1.72	2.01	[0.9- 0.4]	2003-2009
	1,72	1.26	-7.45*	[-2.6- 0.0]	2009-2013
70 - 74 years	2.52	1.63	-2.39*	[-3.1-1.7]	1995-2013
75 - 79 years	2.67	1.67	-2.57*	[-3.3-1.9]	1995-2013
> 80 years	4.98	3.72	-1.60*	[-2.2-1.0]	1995-2013
Total	18.06	11.88	-2.3*	[-2.8 -1.8]	1995-2013

TMEE: Age-standardized mortality rate, estimated in the model
CPA: Annual Percentage Change
* Statistically significant trend

Mortality rates standardized by regions

The highest mortality from gastric cancer in 2013 is concentrated in the central Andes, where the regions of Huancavelica (3.5 times the TMEN), Huánuco (2.5 times the TMEN), Ayacucho and Pasco have the highest mortality, and Junín tops the higher mortality regions. Also, two other high mortality zones are identified: the first in the north of the country (Lambayeque, La Libertad, and Cajamarca) and the second in the central coast (Ica, Callao, Ancash) (see Table 3, Figure 2).

Table 3. Trends standardized mortality rates for gastric cancer by political regions in Peru from 1995 to 2013. Analysis of segmented regress.

Region	TMEE (per 100,000 inhab.)		CPA	CPA	Period	CPAP
	Initial	Final		95% CI		
Amazonas	10.85	21.74	8.0*	[0.0, 16.7]	1995-2004	-0.9
	21.74	5.47	-29.2	[-54.3, 9.7]	2004-2008	
	5.47	9.22	11	[-10.4, 37.4]	2008-2013	
Ancash	15.4	11.98	-1.4	[-3.8, -1.1]	1995-2013	-1.4
Apurímac	7.72	17.24	9.3	[-1.5, 21.3]	1995-2004	0.6
	17.24	8.64	-7.4	[-16.1, 2.3]	2004-2013	
Arequipa	12.38	8.74	-4.8	[-10.1, 0.7]	1995-2002	-3.8
	8.74	11.35	5.4	[-7.9, 20.5]	2002-2007	
	11.35	6.16	-9.7*	[-15.4, -3.5]	2007-2013	
Ayacucho	10.17	19.74	3.8*	[1.3, -6.3]	1995-2013	3.8*
Cajamarca	15.43	22.06	4.1	[-1.6, 10.0]	1995-2004	-1.7
	22.06	12.12	-7.2*	[-11.9, -2.3]	2004-2013	
Callao	18.05	12.46	-2.0*	[-3.5, -0.6]	1995-2013	-2.0*
Cusco	14.42	5.97	-4.8	[-7.1, -2.4]	1995-2013	-4.8
Huancavelica	7.91	37.26	24.8*	[9.8, 41.8]	1995-2002	9.7*
	37.26	41.65	1	[-3.1, 5.3]	2002-2013	
Huánuco	33.13	44.37	2.5	[-0.6, 5.6]	1995-2007	-0.7
	44.37	29.35	-6.7	[-13.4, 0.7]	2007-2013	
Ica	22.09	13.88	-2.6*	[-4.0, -1.0]	1995-2013	-2.6*
Junín	24.19	29.05	3.7	[-7.9, 16.9]	1995-2000	-2.9
	29.05	18.43	-8.7	[-22.5,7.6]	2000-2005	
	18.43	27.73	8.5	[-6.7, 26.2]	2005-2010	
	27.73	14.21	-20	[-38.2, 3.6]	2010-2013	
La Libertad	18.41	23.13	7.9	[-9.1, 28.0]	1995-1998	-1.6
	23.13	13.8	-3.4*	[-4.6, -2.2]	1998-2013	
Lambayeque	16.04	18.57	5	[-27.4, 51.9]	1995-1998	-0.7
	18.57	2.92	-18.6*	[-26.8, -9.5]	1998-2007	
	2.92	13.17	65.1	[-44.8, 393.9]	2007-2010	
	13.17	14.18	2.5	[-23.7, 37.7]	2010-2013	

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Lima	21.54	12.96	-4.1*	[-5.5, -2.7]	1995-2007	
	12.96	15.29	5.7	[-15.2, 31.7]	2007-2010	-3.3
	15.29	11.81	-8.2	[-17.7, 2.3]	2010-2013	
Loreto	13.77	3.28	-7.7*	[-10.7, -4.5]	1995-2013	-7.7*
Madre de Dios	23.22	7.84	-5.9*	[-11.5, 0.1]	1995-2013	-5.9*
Moquegua	15.35	5.69	-5.4*	[-8.4, -2.3]	1995-2013	-5.4*
Pasco	24.55	53.97	48.3	[-17.3, 165.8]	1995-1997	
	53.97	26.43	-21.2	[-55.6, 39.9]	1997-2000	-1.3
	26.43	19.23	-2.4	[-5.3, 0.5]	2000-2013	
Piura	14.87	19.32	14	[-31.7, 90.1]	1995-1997	
	19.32	7.26	-17.8*	[-31.9, -0.8]	1997-2002	-3.3
	7.26	8.09	1	[-2.8, 5.0]	2002-2013	
Puno	10.2	4.96	-3.9*	[-5.7, -2.1]	1995-2013	-3.9*
San Martín	17.46	16.81	-0.3	[-3.3, 2.7]	1995-2006	-3.4*
	16.81	9.42	-7.9	[-13.0, -2.6]	2006-2013	
Tacna	10.61	11.19	0.4	[-2.9, 3.8]	1995-2009	-4.9
	11.19	4.29	-21.3	[-39.1, 1.8]	2009-2013	
Tumbes	18.45	10	-3.4*	[-6.3, -0.3]	1995-2013	-3.4*
Ucayali	18.22	21.84	1.3	[-2.1, 4.8]	1995-2009	-5.4*
	21.84	6.73	-25.51	[-41.2, 5.7]	2009-2013	
Total	18.06	11.88	-2.3*	[-2.8, -1.8]	1995-2013	-2.3*

TMEE: Age-standardized mortality rate, estimated in themodel
CPA: Annual percentage
change CPAP: Average annual percentage change
* Statistically significant trend

REGION	TMEE
Huancavelica	41,65
Huánuco	29,35
Ayacucho	19,74
Pasco	19,23
Junín	14,21
Lambayeque	14,18
Ica	13,88
La Libertad	13,80
Callao	12,46
Cajamarca	12,12
Ancash	11,98
Lima	11,81
Tumbes	10,00
San Martín	9,42
Amazonas	9,22
Apurímac	8,64
Piura	8,09
Madre de Dios	7,84
Ucayali	6,73
Arequipa	6,16
Cusco	5,97
Moquegua	5,69
Puno	4,96
Tacna	4,29
Loreto	3,28
PERU	**11,88**

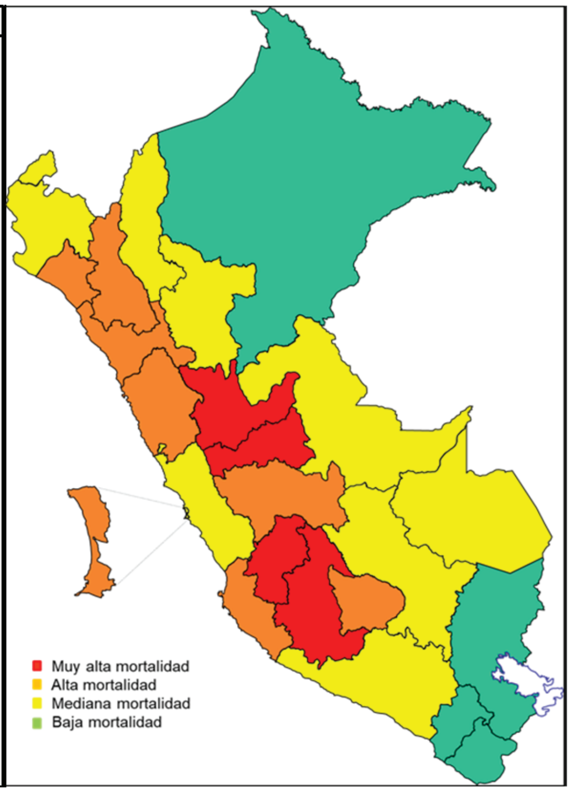

Figure 1. Map of the standardized mortality rates for gastric cancer in Peru estimated by the segmented regression model for the year 2013.

Mortality trends standardized by political regions

Using the interpretation of the annual percentage change proposed by SERGAS (22), the regions were classified according to their estimated standardized mortality trend (using the adjusted segmented regression model) as increasing (CPA ≥1.5%), slightly increasing (0, 5% ≤ CPA <1.5%), stable (0.5% <CPA <0.5%), slightly decreasing (-1.5% <CPA ≤ -0.5%) and decreasing (CPA ≤ -1, 5%). The case of the regions where no joinpoint(s) were found, the CPA value was used. The Average Annual Percentage Change (CPAP) was used in the regions that had one or more joinpoint.

The map shows a growing trend in 2 out of 25 regions, Huancavelica and Ayacucho (CPA: 9.7% and 3.8% respectively). In the Apurímac region a slightly increasing trend is observed (CPA: 0.6%). In 5 regions, the trend is slightly decreasing: Huánuco (CPA: -0.7%), Lambayeque (CPA: -0.7%), Amazonas (CPA: -0.9%), Pasco (CPA: -1.3 %) and Ancash (CPA: -1.4%). in the rest of the 17 out of 25 regions, a decreasing trend is observed (CPA≤1.5%) (see Table 3, Figure 3).

REGION	CPA
Huancavelica	9,7*
Ayacucho	3,8*
Apurímac	0,6
Huánuco	-0,7
Lambayeque	-0,7
Amazonas	-0,9
Pasco	-1,3
Ancash	-1,4
La Libertad	-1,6
Cajamarca	-1,7
Callao	-2,0*
Ica	-2,6*
Junín	-2,9
Lima	-3,3
Piura	-3,3
San Martín	-3,4*
Tumbes	-3,4*
Arequipa	-3,8
Puno	-3,9*
Cusco	-4,8
Tacna	-4,9
Moquegua	-5,4*
Ucayali	-5,4*
Madre de Dios	-5,9*
PERÚ	**-7,7***

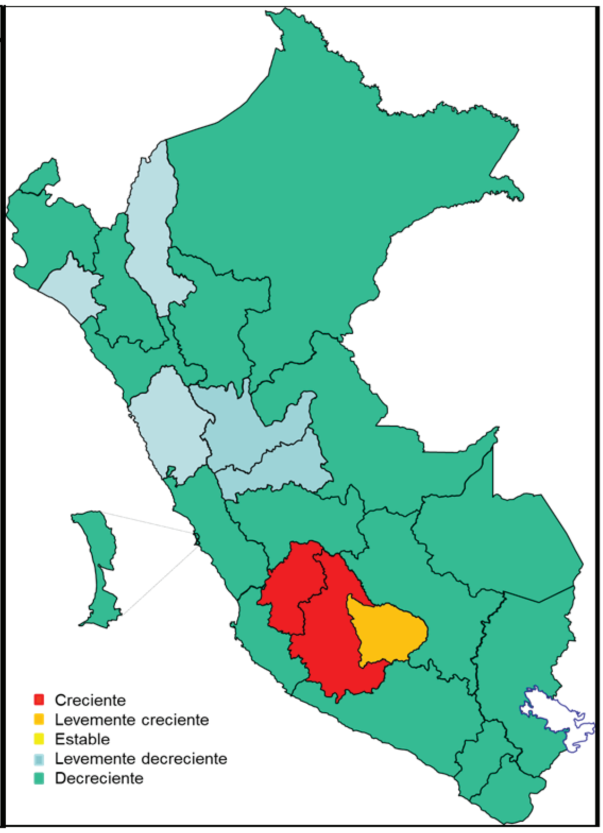

Figure 2. Map of the trends in standardized gastric cancer mortality rates in Peru 1995-2013

In general, in the central Andes area, made up of the Huancavelica, Ayacucho and Apurímac regions, gastric cancer is growing and constitutes the area of greatest risk to die from this disease. The regions with slow decrease are observed in the corridor constituted by the Ancash, Huánuco and Pasco regions, and are also observed in two focal regions with slow decline: Lambayeque and Amazonas (see figure 3).

Table 3 shows the results of the fit of the segmented regression model with the standardized mortality rates estimated at the beginning and at the end of each period of time determined by the joinpoint (s). CPAs are presented for each time segment estimated by the model and for the entire period (CPAP). Are joinpoint (s) to the trend of gastric cancer standardized mortality in the period 1995 to 2013 in 15 of the 25 regions.

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Mortality trends standardized by natural regions

It is observed that the Coast has a growing trend until 1998 (CPA: 1%); then a decreasing one until 2003 (CPA: -6.4%) and then slightly decreasing (CPA: -0.9%). The Peruvian Highlands showed a growing trend until 1997 (CPA: 12.9%). Then it remains stationary until 2009 (CPA: 0%) when it decreases (CPA: -8.3%). The Peruvian Jungle has a decreasing trend until 2009 (CPA: -2.5%) when it becomes more marked (CPA: -12%).

In 1996, the Highlands went from third to second place and it ranks first in mortality from gastric cancer since 1999; the coast that occupied the first place, occupies the second place since 1999, and the Jungle occupies the third place since 1996 (see Table 4).

DISCUSSION

For the year 2012, the standardized gastric cancer mortality rate in developed countries was 9.2 per 100,000 inhabitants and for developing countries, it was 14.4 per 100,000 inhabitants[6]. Peru has experienced in recent years a reduction of 2.3% annually. Under the model studied, it comes closer to developed countries (11.6 per 100,000 inhabitants), occupying in the region of the Americas the 6th place, surpassed by Guatemala, Ecuador, Honduras, Chile and El Salvador[2,3].

An investigation of the standardized gastric cancer mortality rates in Peru from 2005 to 2014 carried out by Hernández-Vásquez et al., shows a reduction from 15.49 to 12.13 per 100 000 inhabitants[12]. The disadvantage of this graphic analysis is the insufficiency to study the temporal evolution of numerical series since it does not allow characterizing the phenomenon due to the distortions presented by the annualized data, which is eliminated by using generalized linear models that allow a more objective analysis. A longer series from 1986 to 2015 on gastric cancer mortality in Peru shows a reduction of 40%, with a constant rate of 2% per year[24]. However, this trend was calculated by adjusting log-linear models with the Poisson distribution. In these models a canonical link function is used, and the data is aggregated, stratified by age groups and year of death. Unlike these studies, our work analyzes the logarithm of the standardized rates using linear regression models by segments that have the advantage of conducting a study stratified by subgroups and identifying sudden changes in the trend.

In Latin America, a decreasing trend is observed in gastric cancer mortality[25]. In Peru this decreasing trend is similar to the ones observed in Asian or Eastern European countries[26]. Decreasing trends in stomach cancer mortality have also been documented in regions with historically high rates, including countries in Asia (Japan, China, and Korea)[3], Latin America[25], and Europe (Ukraine)[3]. The factors that have contributed to this decline are attributed to the increased availability of fresh produce, fruits and vegetables, less dependence of canned food on salinity, and the reduction in chronic H. pylori infection due to better sanitation and antibiotics[10].

In Peru, the decrease in mortality from this cancer, according to various authors, could be attributed to improvements in the population's living conditions, such as the use of safe water, provision of adequate sanitation or sewerage systems, and cooling of foods[15], factors that contribute to reduce the transmissibility of Helicobacter pylori, more than the medical progress aimed at treating gastric cancer cases, since there is a huge gap in cancer services in the country[8].

Since 2001, Kaneko and Yoshimura postulate that the decrease in intestinal-type gastric cancer incidence is the factor that most contributes to the decrease in the incidence of gastric cancer worldwide[27]. However, Henson et al. (2004), point out that the incidence of diffuse-type gastric carcinoma, particularly the signet ring type, has been increasing[28].

Chronic H. pylori infection is the identified risk factor with strongest association to stomach cancer, with approximately 90% of new cases of non-cardiac gastric cancer worldwide cases[11]. Ramirez Ramos et al. (2003) conducted a study of variation in the prevalence of infection H. pylori in Peru between 1985 and 2002, with reference to the population of a clinic in Lima Metropolitana which was considered medium and high socioeconomic. It was found that in 1,260 patients with active chronic gastritis a prevalence of H. pylori that decreased from 83.3% to 58.7% (p-value <0.001), being more significant in those under 30 years of age. In 178 patients with duodenal ulcer it decreased from 89.5% to 71.9% (p value = 0.004), but there were no statistically significant differences in patients with gastric ulcer or normal mucosa[29]. In general, is observed a decrease in the prevalence of H. pylori in the different Peruvian studies carried out[30].

52.1% of deaths from gastric cancer in Peru occurred in men, which is lower than that reported worldwide. In 2012, it was estimated that 64.9% of deaths from gastric cancer occurred in men and developing countries reported 66.1%[6]. A recent study on the trend in gastric cancer mortality in Peru from 2003 to 2016, which uses the classic non-parametric Mann-Kendall trend test to check whether there is a trend in the time series, shows a decrease in the proportion of Deaths attributed to gastric cancer in those over 50 years statistically significant for men from 25.7% to 21.8% and for women from 24.4% to 16.44%[31]. Another study analyzed the histological type of 3568 patients with gastric cancer registered in the National System of Epidemiological Surveillance of cancer of the Ministry of Health between the years 2009-2010 and 43.2% were of unspecified type, 33.6% of intestinal type (the most related to Helicobacter pylori) and 18.7% of diffuse type. A higher prevalence of the diffuse type is observed in women, 21.6% versus 16% in men, and in general, a higher percentage compared to that reported in the literature, which could explain why gastric cancer in Peru occurs in a almost 1:1 ratio of men to women[14].

This study finds an increase in the gastric cancer mortality rate adjusted by age group as it increases (see Table 1), as reported in the literature. In the age segment of 40-44 years for the Americas region in 2012 the rate was 3.9 per 100,000 inhabitants. and it increases to 64.9 per 100,000 inhabitants. for the age group from 70 to 74 years[23].

Higher gastric cancer mortality in Peru is concentrated in the central Andes, this scenario is constituted by the regions of Huancavelica, Huánuco, Ayacucho, Pasco and Junín. The second high mortality scenario is found in the north of the country (Lambayeque, La Libertad and Cajamarca), the third in the central coast (Ica, Callao, Ancash and Lima) (see figure 2). Piñeros et al. (2017) have also noted this pattern that attests a positive correlation between altitude and gastric cancer. However, it has been suggested that altitude is a proxy for factors that could be grouped into mountainous regions- for example, host genetic, bacterial, dietary, and environmental factors[32]. Local studies in Lima reported a positive association between ethnic descent and stomach cancer, and a predominant role for socioeconomic factors associated with ethnicity and disparities in access to health services[33].

The United Nations Development Programme (2013) reports shows that Peru reached an HDI of 0.74 and regions with the lowest HDI were Huancavelica with 0.297; then Ayacucho with 0.334, Apurimac with 0.344 and Huánuco with 0.374[34]. This finding postulates the hypothesis that poor conditions of poverty, education, and sanitation would contribute to higher mortality from gastric cancer, possibly due to greater transmissibility and chronicity of H. pylori infection, as well as, less access to health services. Bray also points out this in the publication of global cancer trends for the period 2008-2030[35].

Regarding the socio-economic level and after reviewing studies in various care centers for patients of socioeconomic level medium and high Ramírez Ramos et al. (2006) points out that there is a significant decrease in the prevalence of H. Pylori infection (45%) compared to 80% observed a decade ago[29].

One of the most important factors for the decreasing trend in gastric cancer mortality in Peru could be the substantive improvement in living conditions that reduces the transmissibility of infection by helical pylori: a) between 2001 and 2014, the percentage of rural households with drinking water in their home from 35.1 to 61.8%[15], b) A reduction of 12.4 percentage points in the number of homes with poor excreta disposal from 2001 to 2014 is documented, being more substantive at the rural level. it was significantly reduced from 49.8 to 24%[15].

However, from 1995 to 2015 the standardized mortality rate reported by the Ministry of Health of Peru increased from 18.4 per 100,000 inhabitants at the rural level to 30.9 per 100,000 inhab. While in urban areas it was reduced from 32.3 per 100,000 inhabitants to 17.7 per 100,000 inhab.[24]. This migration of mortality from gastric cancer could be due to problems of timely access to health services, since cancer treatment centers are all located in urban areas. As well as access to diagnosis by endoscopy, although it is not very widespread, it is carried out almost entirely in urban areas[8]. In accordance with what was reported by Pereira et al., Who pointed out that the rural area encompasses socioeconomic factors associated with ethnicity and disparities in access to health services[33].

In the present study it is also observed changes in gastric cancer mortality trends by natural regions that are in accordance with rurality, since the mountains and jungle concentrate the regions with the highest rurality with respect to the coast. This explains why in 1995 the Coast had the highest mortality and in 2013 the Highlands was the one with the highest mortality, it is important to propose targeted socio-sanitary

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studies to test the hypothesis regarding whether the lower migration of the inhabitants of rural areas of the sierra, genetic and environmental conditions and inequities in access to health services explain the higher mortality from gastric cancer.

LIMITATIONS

One of the main limitations of the research is the under-reporting of the database of deaths of vital statistics of the Ministry of Health. Another limitation is the period analyzed between 1995 to 2013, since it is possible that there are changes in the trends of the successive years, however, a great amount of years is required to have the consistent final data and to be incorporated into the segmented regression model.

CONCLUSION

The trend in stomach cancer mortality in Peru is decreasing and statistically significant for the period 1995 - 2013 (-2.3% per year). Different behavior due to sex, age groups, political and georgafical groups are observed. The departments with an increasing mortality trend are Huancavelica, Ayacucho and Pasco in the central Andes. A greater reduction in SMD is observed in women compared to men.

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