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GASTRIC CANCER AND ANEMIA IN THE ECUADORIAN ANDES

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ABSTRACT

INTRODUCTION: Gastric cancer is the second most common cause in incidence of malignancy in Ecuador, the purpose of this investigation is to determine the overall survival of patients with gastric cancer living at 2000 meters above the sea level.
METHODOLOGY: A cohort-retrospective study was conducted at the "General Solón Espinosa Ayala Oncology Hospital" of those patients diagnosed with gastric cancer stages IB to IIIC according to the AJCC seventh edition, during the period of 2011 to 2015, evaluating the overall survival using Kaplan Meyer curves, Long Rank, as well as a general descriptive analysis.
RESULTS: The overall survival of patients with anemia prior to surgery was distributed as follows, patients without anemia 56.4 months; mild anemia 31.4 months and moderate anemia 26.6 months with a Long Rank of 0.563 p = 0.453; for patients who completed concomitant adjuvant chemo-radiotherapy treatment according to the Intergroup 0116 study; that mentioned that not having anemia but having a low mean corpuscular volume represents greater survival than those without anemia but its average corpuscular volume is normal, with a global survival of 56.4 months in patients with low corpuscular volume vs 43.8 months for those with corpuscular volume normal; Long Rank of 0.657 p = 0.41
DISCUSSION: Although the results obtained were not statistically significant, we can observe that the patients who did not have anemia had a greater survival than those who do, and it is very striking that of the group of patients who did not have anemia but their average corpuscular volume was low. had greater survival, perhaps this is due to a phenomenon called eryptosis that showed that in the oncological patient the concentration of hemoglobin and cell volume is significantly lower than in the healthy patient, indicating that despite an increase in the values of phosphatidylserine in the erythrocyte there was no increase in erythropoiesis.

INTRODUCTION

Gastric cancer is the second cause of incidence in Ecuador and the leading cause of mortality in men according to our national tumor registry in Quito 2014 (1). Its incidence is greater in developing countries compared to developed countries; However, it should be noted that three countries account for 60% of gastric cancer in the world: China, Korea and Japan. (2-5)

For Montero et al; From 2004 to 2007 and from 2008 to 2011, the provinces with the highest indirect standardized mortality rates were Carchi; and from 2012 to 2015, were the provinces of Cotopaxi, Bolívar, Los Ríos, Chimborazo and Tungurahua with a relative risk of 1.34 p = <0.001; provinces with an overall height greater than 2200meters above sea level; the spatial analysis indicates the presence of high occurrence clusters of gastric cancer in the entire Cordillera de los Andes. (6)

People living at a certain altitude above sea level increase hemoglobin concentrations, therefore, in people who live at high altitudes, the prevalence of anemia can be underestimated if the cut-off values are corresponding to a height at the level of the sea (7)

On the other hand anemia is a disorder in which the number of erythrocytes, and consequently, the oxygen transport capacity of the blood is insufficient, (7-9), can be caused by iron deficiency, Vitamin B12 or both , being frequently after gastrectomy, (7,10) this deficiency can be a result of malabsorption, chronic bleeding, and vitamin B12 deficiency due to the lack of intrinsic factor.

Previous studies have shown that the lower the erythrocyte distribution count, the lower the survival, but with certain background limitations (10), the primary end point of the investigation was to determine the overall survival of patients diagnosed with gastric cancer at a height greater than 2000. meters above sea level related to hemoglobin levels.

METHODOLOGY

A cohort-retrospective study was conducted at the "General Solón Espinosa Ayala Oncology Hospital" of those patients diagnosed with gastric cancer clinical stages IB to IIIC according to the 7th edition of the AJCC, went to gastrectomy as first step and then received adjuvant treatment with chemotherapy and radiotherapy at the same time according to the Intergroup 0116 study; During the period of 2011 to 2015, the data was collected from the electronic medical records of the institution in Microsoft Excel 2010 program and the data were analyzed in the SPSS Version 21 program, the findings were analyzed in a descriptive way. Kaplan Meyer's survival of patients also were analized

The concept of anemia was defined according to the World Health Organization (WHO) as a level of Hemoglobin (Hb) <12 g / dL in women and <13 g / dL men) (7-13)

The hematimetric indices allow a morphological classification of the anemias, when the indices are diminished, we refer of microcytic and hypochromic anemias, as is the case of ferropenic anemias, thalassemias, sideroblastic anemias and chronic processes.

Iron-deficiency anemia is characterized by low iron levels, increased transport capacity, decreased transferrin saturation, low serum ferritin. (14,15)

Normocytic, normochromic anemias are often due to hemolysis or acute hemorrhage. (9.16)

A high mean corpuscular volume (MCV) and wide distribution of normal erythrocytes (ADE) is almost exclusive of a myelodysplastic syndrome. (17,18)

Megaloblastic anemias, if there is iron deficiency associated, reticulocytes are usually low, otherwise they may be within normal but never increased except in treatment (9)

Megaloblastic anemia, on the other hand, are characterized by decreased levels of serum vitamin B12, normal or increased serum folate, and decreased intraerythrocytic folate, which are observed in vitamin B12 deficiency (9,13,19).

WHO proposes that Hemoglobin values should be adjusted at high altitude, however there is evidence to suggest that it should not be necessary, since there is no agreement between the frequency of anemia at presentation in height when it is based on the measurement of Hemoglobin corrected for altitude or by the body iron content (7.8)

The process in the laboratory, the reading of hemoglobin and hematocrit at the oncological hospital "Solón Espinosa Ayala" is provided by 2 machines; a SYSMEX XT1800i and the XN1000 with a margin of error of less than 5% (20,21)

RESULTS

133 individuals were analyzed, distributed in 80 men and 53 women with range of age from 13 to 89 years, with a mean age of 61 years, with a diagnosis of gastric cancer, clinical stages IB to IIIC according to the AJCC seventh edition, and its data were collected thanks to the National Registry of Tumors of SOLCA-QUITO including records during the years 2011 to 2015

The overall survival of men in relation to women was evaluated first, resulting in greater survival in favor of women 56.5 months vs 38.7 months, with a long rank of 1,285 p = 0.257 as shown in figure 1.

The condition of anemia prior to surgery was first evaluated, identifying that 27.8% corresponded to a degree of anemia while 72.2% of individuals did not have anemia, as described in Table 1.

Of the individuals with anemia prior to surgery; The overall survival of patients who did not have anemia was 56.4 months; mild anemia 31.4 months and 26.6 months for moderate anemia, on the other hand the average survival of 15.9 months for those without anemia, 14 months for those who have mild anemia and 12.8 months for those with moderate anemia, with a Long Rank of 0.563 p = 0.453 as shown in figure 2.

The overall survival of the individuals according to the type of anemia was 43.8 months for normocytic anemia; microcytic anemia 34.7 months, with an average survival of 15.74 months for those with normocytic anemia and 13.60 months for those with microcytic anemia, Long Rank of 1.199; p = 0.27 as shown in Figure 3.

For the patients who completed the chemotherapy-radiotherapy adjuvant treatment according to the Intergroup 0116 study, (22) the results were obtained, the individuals who do not have anemia but whose volume is corpuscular medium is microcytic that presents anemia survival than those who do not have anemia but its mean corpuscular volume is normal, with a global survival of 56.4 months in patients with small cell volume versus 43.8 months with normal corpuscular volume; Long Rank of 0.657 p = 0.41. As shown in figure 4.

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Patients who completed adjuvant treatment of chemotherapy-radiotherapy according to the Intergroup 0116 trial, (22) the following results were obtained: individuals who did not have anemia but whose mean corpuscular volume was microcytic showed higher survival than those who did not have anemia but its mean corpuscular volume was normal, with a overall survival of 56.4 months in patients with microcytic mean corpuscular volume vs 43.8 months for those with normal corpuscular volume; Long Rank of 0.657 p = 0.41. As shown in figure 4.

DISCUSSION

There are few articles and trials that describe the relationship of gastric cancer and high altitude, perhaps one of the few of them is described by Chirino et al; who mentioned that two thirds of patients with gastric cancer have migrated from the highlands of Peru (+/- 3000m), although this finding is associated with socioeconomic conditions and poverty, for our part this relationship has not yet been described and we analyzed in this study patients who live at a higher altitude more than 2000 meters above sea level.

Simeonov et al, describes the relationship among barometric pressure, oxygen and high altitude indicating that at sea level the partial pressure of oxygen decreases in relation to high altitude, reaching 78.5% at 2000 meters; this may explain that the lower the amount of oxygen, the lower the possibility of forming oxygen-free radicals that cause cell damage, maybe a negative fact in this study is the absent description of gastric cancer, but in our work we have sought to associate the high altitude, hemoglobin value and Survival in patients with gastric cancer.(23,24)

Although the present study has shown to be not statistically significant and demonstrate that there is no relationship between high altitude and gastric cancer accompanied by anemia, interesting survival curves are observed, such as one in which a patient without anemia but with a low Mean Corpuscular Volume lives longer than those without anemia but with normal mean corpuscular volume; perhaps this can be explained by the concept called eryptosis; phenomenon that was first discussed in lung cancer and myelodysplastic syndrome, which showed that the concentration of hemoglobin and cell volume is significantly lower than healthy patient, showing that despite an increase in the values of phosphatidylserine in the erythrocyte there was no increase in erythropoiesis.

The stimulation of the eryptosis in cancer is presumably increased by the deficiency of iron and this in turn is associated with oxidative stress, we have to consider that this scenario is increased with cytostatic chemotherapy(11)

It is interesting to see the survival graph in relation to anemia prior to chemotherapy treatment, there is a cross-over from the twentieth month, clarifying that this group of patients did not have anemia but their average corpuscular volume remained low, they had better survival and maybe the fact of a chance of influence of the high altitude in a certain degree with respect to this parameter, it could also be concluded that a deficiency factor is involved later and motivates its better survival, However we need more trails and research comparing high altitude and all the implications related to anemia, we can recommend to keep Hemoglobin levels greater than 12g / dL to improve survival in patients with gastric cancer.

As weak points in this investigation, our research is a retrospective study and that in the future it would be interesting to prospectively investigate this topic in relation to more hematological variables that may affect survival.

TABLA 1.- The condition of anemia prior to surgery

VARIABLE		n	%	p
Gender	Male	80	60,2	
	Female	53	39,8	
	Total	133	100	
Age	Minimum	13		
	Mximum	89		
Clinical Stage	EIB	12	9	
	EIIA	16	12	
	EIIB	14	10,5	
	EIIIA	16	12	
	EIIIB	42	31,6	
	EIIIC	33	24,8	
Mild Anemia previous to surgery	Men	12	15,2	0.13
	Women	7	13,5	
	Total	19	14,5	
Moderate Anemia previous to surgery	Men	10	12,7	0.13
	Women	6	11,5	
	Total	16	12,2	
No anemia	Men	57	72,2	0.13
	Women	39	75	
	Total	96	73,3	

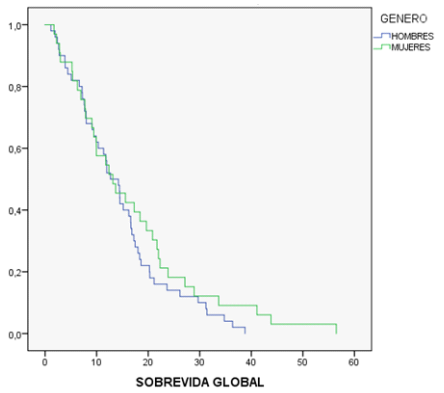

FIGURE 1. The overall survival of the individuals according to the type of anemia prior to gender

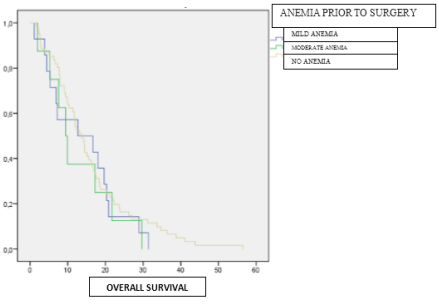

FIGURE 2. The overall survival of the individuals according to the type of anemia prior to surgery

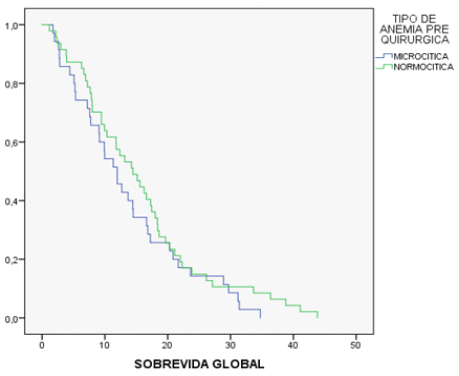

FIGURE 3.- The overall survival of the individuals according to the type of anemia prior to surgery

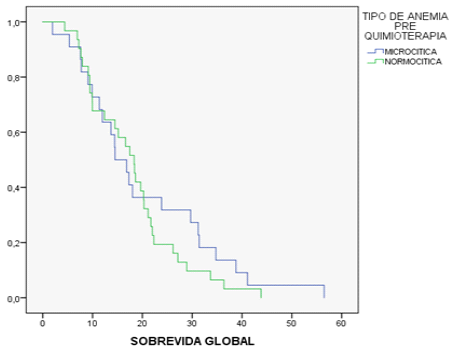

FIGURE 4.- The overall survival of the individuals according to the type of anemia prior to chemotherapy

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