

## Risk of death from congestive heart failure among Peruvian patients with anemia

Alberto Guevara Tirado\*<sup>1,2,a,b</sup>

### ABSTRACT

**Objective:** To determine the risk of death from underlying congestive heart failure among Peruvian patients with anemia.

**Materials and methods:** An observational, descriptive, case-control and retrospective study based on data from the Sistema Informático Nacional de Defunciones (SINADEF - National Death Computer System) of the Ministry of Health of Peru (MINSa) and conducted between January 2021 and August 2022. A non-probability purposive convenience sampling was used considering the inclusion and exclusion criteria. All patients with and without anemia who died from congestive heart failure or other comorbidities were included in the research, totaling 35,724 people. The variables were anemia, defined as a condition related to the amount or number of red blood cells and hemoglobin, as well as to iron absorption and availability, and congestive heart failure, defined as the inability of the myocardium to pump blood efficiently. Chi-square test and phi and Cramér's V coefficients were used to determine the presence and degree of association of the variables and the odds ratio for risk estimation. A significant  $p$  value less than 0.05 with a 95 % confidence interval was considered.

**Results:** Anemia was moderately associated with congestive heart failure: 62.80 % of people with anemia died from this disease. The variables were statistically related and, according to phi and Cramér's V coefficients, there was a moderate relationship. People with anemia had 11.14 times higher risk of dying from congestive heart failure than people with other comorbidities.

**Conclusions:** Anemia is associated with high risk of death from underlying heart failure in the Peruvian population. It is necessary to monitor iron, hemoglobin and red blood cell levels among patients with heart failure, as well as to identify the causes of these deficiencies in order to reduce morbidity and mortality in this group of patients.

**Keywords:** Heart Failure; Anemia; Chronic Disease; Cause of Death; Odds Ratio (Source: MeSH NLM).

## Riesgo de muerte por insuficiencia cardiaca congestiva en pacientes anémicos de la población peruana

### RESUMEN

**Objetivo:** Determinar el riesgo de muerte por insuficiencia cardiaca congestiva subyacente en pacientes anémicos de la población peruana.

**Materiales y métodos:** Estudio observacional, descriptivo, de casos y controles y retrospectivo basado en datos del Sistema Informático Nacional de Defunciones (Sinadef) del Ministerio de Salud (Minsa) peruano entre enero de 2021 y agosto de 2022. El muestreo fue no probabilístico, intencional por conveniencia según los criterios de inclusión y exclusión. Se incluyó a todos los pacientes con y sin anemia que fallecieron por insuficiencia cardiaca congestiva u otras comorbilidades, que sumaron un total de 35 724 personas. Las variables fueron anemia, definida como un trastorno del tamaño o número de hematíes, de la hemoglobina, así como de la absorción y disponibilidad del hierro, e insuficiencia cardiaca congestiva, definida como la incapacidad del miocardio para bombear sangre de forma competente. Se realizó la prueba de chi al cuadrado y de los coeficientes Phi y V de Cramer para determinar la existencia y grado de asociación de las variables y la razón de probabilidades para la estimación del riesgo. Se consideró un valor de  $p$  significativo menor del 0,05, con un intervalo de confianza al 95 %.

**Resultados:** La anemia estuvo moderadamente asociada a la insuficiencia cardiaca congestiva: fallecieron 62,80 % de personas con anemia. Las variables están estadísticamente relacionadas y, según los coeficientes Phi y V de Cramer, se trata de una relación moderada. Se halló que los anémicos tuvieron 11,14 veces mayor riesgo de morir por insuficiencia cardiaca congestiva que las personas con otras comorbilidades.

**Conclusiones:** La anemia se asocia a un alto riesgo de muerte por insuficiencia cardiaca subyacente en la población peruana. Es necesario el seguimiento de los niveles de hierro, hemoglobina y hematíes en pacientes con insuficiencia

1 Universidad de San Martín de Porres, School of Human Medicine. Lima, Peru.

2 Universidad Privada del Norte, School of Human Medicine. Lima, Peru.

a Doctor of Medicine.

b Master's degree in Medicine.

\*Corresponding author.

cardiaca, así como tratar las causas de estas deficiencias, con el objetivo de reducir la morbimortalidad en este grupo de pacientes.

**Palabras clave:** Insuficiencia Cardiaca; Anemia; Enfermedad Crónica; Causas de Muerte; Oportunidad Relativa (Fuente: DeCS BIREME).

## INTRODUCTION

Congestive heart failure is a condition caused by impaired cardiac pumping <sup>(1)</sup>. It can be caused by ischemic heart diseases, myocardial infarction, hypertension, valvular heart diseases, alcoholism, infections, among others <sup>(2)</sup>. It is a costly and high-mortality disease with a risk of death similar to that of some neoplasms <sup>(3)</sup>. Its prevalence rates are increasing worldwide, thus being considered a global epidemic with 17 million deaths per year <sup>(4)</sup>. It affects approximately 64 million people <sup>(5)</sup>, mainly in developed countries such as the United States, where almost 6 million people and 550,000 new cases per year suffer from this disease <sup>(6)</sup>. However, in developing countries, its occurrence increasingly growing due to the higher rate of life expectancy and diseases such as diabetes, hypertension, dyslipidemia and obesity <sup>(7)</sup>. Its prevalence is increasing in Peru, especially in adults aged over 65 years, with high mortality rates in the first year (70 %) <sup>(8)</sup>.

The adverse role of anemia in heart failure, which leads to a hyperhemodynamic state, has been widely studied <sup>(9)</sup>. In addition, the excess of compensatory cardiac work to provide oxygen to the body affects the sympathetic nervous activity and tone <sup>(10)</sup>, thus contributing to myocardial remodeling <sup>(11)</sup>.

Additionally, it has been suggested that gastrointestinal edema affects iron absorption <sup>(12)</sup>, which is also affected by inflammatory cytokines—including interleukins 1 and 6—together with tumor necrosis factor alpha <sup>(13)</sup>, which promote iron storage in the reticuloendothelial system <sup>(14)</sup> and affect its utilization. Moreover, interleukin 6 would affect erythropoiesis in the bone marrow <sup>(15)</sup>. On the other hand, it has been observed that folic acid or vitamin B12 deficiency does not significantly contribute to anemia associated with heart failure <sup>(16)</sup>. Likewise, the role of angiotensin II in red blood cell production—either by stimulation of erythropoiesis or by direct effects on erythropoiesis in the bone marrow—has been proposed, although there is still no consensus on this topic <sup>(17)</sup>. The coexistence of heart failure and chronic renal disease increases the risk of anemia; it has been observed that reduced hemoglobin levels are similar to reduced glomerular filtration rates <sup>(18)</sup>. Possible iatrogenic mechanisms such as the use of antithrombotic drugs, which might cause minor gastrointestinal bleeding that could contribute to anemia, have also been proposed <sup>(19)</sup>.

In spite of several studies on the influence of anemia on morbidity and mortality in heart failure, there is no agreement on the prognostic value of this disease <sup>(20)</sup>. Research on congestive heart failure in Peru, mainly aimed at understanding the clinical course of the disease, has increased in the last 20 years <sup>(21)</sup>. Therefore, the objective of the present research is to determine the risk of death from congestive heart failure among patients with anemia. This will allow us to establish its impact on mortality among patients with low red blood cell count: an issue that is still in search of consensus in the international medical community and that has been little researched in the Peruvian population.

## MATERIALS AND METHODS

### *Study design and population*

A descriptive, cross-sectional, retrospective, case-control study consisting of all deceased patients between January 2021 and August 2022 whose comorbidity was anemia and whose cause of death was divided into congestive heart failure and other conditions, according to the database of deaths of the Sistema Informático Nacional de Defunciones (SINADEF - National Death Computer System) of the Ministry of Health of Peru (MINSA). No formula was employed, since the entire available population—totaling 35,724 deceased patients—was studied. A purposive, non-probability, convenience sampling was used based on the inclusion and exclusion criteria. People with or without anemia registered in SINADEF were included, as well as those who mainly died from congestive heart failure and also from other comorbidities. Moreover, subjects with no study variables or with incomplete data, as well as individuals whose immediate cause of death or comorbidity was suspected, confirmed or related to COVID-19 disease, were excluded.

### *Variables and measurements*

One variable was anemia, defined as a condition related to the amount or number of red blood cells and hemoglobin, as well as iron absorption and availability <sup>(22)</sup>; no distinction was made according to the type or origin. The other variable was congestive heart failure, defined as the inability of the myocardium to pump blood efficiently <sup>(23)</sup>. A documentary analysis was performed, as the database records were reviewed to screen the cases relevant to the research.

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### Statistical analysis

IBM SPSS (Statistical Package for Social Sciences) Statistics V25 for Windows was used. Regarding the analytical statistics, the following tests were performed: Pearson's chi-square test to assess the statistical association, phi and Cramér's V correlation coefficients to determine the degree of association, and the odds ratio to establish the risk of death from vascular disease in the group of patients with anemia (cases) and patients without anemia with other comorbidities (controls) in comparison with a group that died from congestive heart failure and a group that did not die from this condition. The findings were measured at a significant *p* value less than 0.05 with a 95 % confidence interval.

### Ethical considerations

The open-access database did not include personal data; therefore, encoded data was stored anonymously.

### RESULTS

Congestive heart failure was the immediate cause of death in 62.80 % of patients with anemia in contrast to 13.20 % of those who died without recorded anemia (Table 1).

**Table 1.** Contingency table of the relationship between anemia and death from congestive heart failure

		Death from congestive heart failure		
		Yes	No	Total
With anemia	<i>n</i>	630	373	1003
	%	62.80	37.20	100
Without anemia	<i>n</i>	4,571	30,150	34,721
	%	13.20	86.80	100
Total	<i>N</i>	5,201	30,523	35,724
	%	14.60	85.40	100

The variables were statistically related and, according to phi and Cramér's V correlation coefficients, there was a moderate relationship. People with anemia had 11.14 times higher risk of dying from underlying congestive heart failure (Table 2).

**Table 2.** Degree of association and risk of death from congestive heart failure among Peruvian patients with anemia

	<i>N</i>	OR	95 % CI	Phi	Cramér's	<i>p</i>
Anemia-CHF	35,724	11.14	9.76-12.71	0.23	0.23	0.000

CHF: congestive heart failure; *N*: number; OR: odds ratio; CI: confidence interval; *p*: asymptotic significance.

Source: self-elaboration.

### DISCUSSION

Anemia was moderately and positively associated with death from congestive heart failure, and the rate of death was high compared with that of patients with comorbidities other than anemia. This agrees with Abebe et al. who, in a study on the prevalence of anemia among patients with heart failure and on the outcomes of patients with severe heart failure with and without anemia admitted to a hospital in Ethiopia, found a prevalence of 45 % of patients with anemia and heart failure <sup>(24)</sup>. Ikama et al., in a study on the prevalence of anemia among patients with heart failure conducted in a university hospital in Congo, estimated a prevalence of 42 % <sup>(25)</sup>. Cleland et al., in a study on the prevalence and outcome of anemia and hematinic deficiencies

among patients with chronic heart failure, found that 68 % of the patients had anemia and congestive heart failure <sup>(26)</sup>. In general, the actual frequency of anemia among patients with heart failure depends on the definition and ranges according to the particular population and demographics of each country. The cut-off point for delimiting normal values and anemia is the one defined by the World Health Organization (WHO) <sup>(27)</sup>, which is a generalized value that does not consider a specific adjustment for congestive heart failure; i.e., the definition of anemia by the WHO has not been validated for patients with congestive heart failure.

Patients with anemia had a high risk of dying from underlying heart failure. The results agree with the study by Casas et

al. who, in an article on anemia as a predictor of heart failure mortality in a hospital in Lima, Peru, found 2.82 times higher probability of death from congestive heart failure in those who had anemia <sup>(28)</sup>. Armas et al., in an article aimed to determine the association between anemia and cardiovascular mortality 30 days after admission for heart failure in an emergency hospital in Peru, found 3 times higher risk of death in the presence of anemia <sup>(29)</sup>. Romero et al., in a study on anemia as a risk factor for mortality among patients with heart failure hospitalized in Trujillo, Peru, found 5 times higher risk of death among patients with anemia <sup>(30)</sup>. The preceding research works agreed that a relationship exists. However, the absolute and relative risks were lower than those found in the present study, where there was an 11 times higher absolute risk of death. This could be due to the methodological design and the sample size of this research since it consisted of a population of 35,724 people, out of whom 1,003 had anemia, compared to the abovementioned studies whose sample size was around 100 patients.

The limitations of this study were related to the methodological design: there was no sample calculation since the entire available population was included in the research based on the inclusion criteria; i.e., convenience sampling was used. Moreover, due to the nature of the data source, it is possible that there were other comorbidities in addition to anemia and heart failure which were not recorded in the SINADEF and could have caused complications and accelerated death.

In conclusion, anemia increases the risk of death from congestive heart failure in the Peruvian population. It is necessary to monitor iron, hemoglobin and red blood cell levels among patients with heart failure, as well as to identify the causes of these deficiencies, in order to reduce morbidity and mortality associated with congestive heart failure in this group of patients.

**Acknowledgements:** We thank MINSAs SINADEF, whose open-access website data allowed the development of this research.

**Author contributions:** The author developed, wrote and reviewed this research study.

**Funding sources:** The article was funded by the author.

**Conflicts of interest:** The author declares no conflicts of interest.

## BIBLIOGRAPHIC REFERENCES

- Schwinger RHG. Pathophysiology of heart failure. *Cardiovasc Diagn Ther.* 2021;11(1):263-76.
- Slivnick J, Lampert BC. Hypertension and heart failure. *Heart Fail Clin.* 2019;15(4):531-41.
- Vallabhajosyula S, Jentzer JC, Geske JB, Kumar M, Sakhuja A, Singhal A, et al. New-onset heart failure and mortality in hospital survivors of sepsis-related left ventricular dysfunction. *Shock.* 2018;49(2):144-9.
- Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur J Heart Fail.* 2020;22(8):1342-56.
- Joseph P, Dokainish H, McCreedy T, Budaj A, Roy A, Ertl G, et al. A multinational registry to study the characteristics and outcomes of heart failure patients: The global congestive heart failure (G-CHF) registry. *Am Heart J.* 2020;227:56-63.
- Johansson I, Joseph P, Balasubramanian K, McMurray JJV, Lund LH, Ezekowitz JA, et al. Health-related quality of life and mortality in heart failure: The Global Congestive Heart Failure study of 23 000 patients from 40 countries. *Circulation.* 2021;143(22):2129-42.
- Chamberlain AM, Boyd CM, Manemann SM, Dunlay SM, Gerber Y, Killian JM, et al. Risk factors for heart failure in the community: Differences by age and ejection fraction. *Am J Med.* 2020;133(6):e237-48.
- Villar MR, Valdez J. Características epidemiológicas y clínicas de la insuficiencia cardíaca aguda en un hospital de referencia, Arequipa, Perú 2017 - 2018 [Internet] [Undergraduate thesis]. [Arequipa]: Universidad Católica de Santa María; 2019. Available from: <https://repositorio.ucsm.edu.pe/handle/20.500.12920/8693>
- Alnuwaysir RIS, Hoes MF, van Veldhuisen DJ, van der Meer P, Grote N. Iron deficiency in heart failure: Mechanisms and pathophysiology. *J Clin Med.* 2021;11(1):125.
- Hamed SA, Elhadad AF, Abdel-aal RF, Hamed EA. Cardiac autonomic function with iron deficiency anemia. *J Neurol Exp Neurosci.* 2020;6(2):51-7.
- Konstam MA, Kramer DG, Patel AR, Maron MS, Udelson JE. Left ventricular remodeling in heart failure: current concepts in clinical significance and assessment. *JACC Cardiovasc Imaging.* 2011;4(1):98-108.
- Martens P. The effect of iron deficiency on cardiac function and structure in heart failure with reduced ejection fraction. *Card Fail Rev.* 2022;8:e06.
- Siddiqui SW, Ashok T, Patni N, Fatima M, Lamis A, Anne KK. Anemia and heart failure: A narrative review. *Cureus.* 2022;14(7):e27167.
- Anand I, Gupta P. How I treat anemia in heart failure. *Blood.* 2020;136(7):790-800.
- Beverborg NG, van Veldhuisen DJ, van der Meer P. Anemia in heart failure: Still relevant? *JACC Heart Fail.* 2018;6(3):201-8.
- Arora H, Sawhney JPS, Mehta A, Mohanty A. Anemia profile in patients with congestive heart failure a hospital based observational study. *Indian Heart J.* 2018;70(Suppl 3):S101-4.
- Jonaitienė N, Ramantauskaitė G, Laukaitienė J. Anaemia in heart failure patients, associated with angiotensin - renin - aldosterone system altering medications. *Heart Views.* 2021;22(3):196-200.
- Okuno K, Naito Y, Asakura M, Sugahara M, Horimatsu T, Yasumura S, et al. Anemia has an impact on prognosis in heart failure with preserved ejection fraction with mild chronic kidney disease. *Int J Cardiol Heart Vasc.* 2021;34(100796):100796.
- Sîrbu O, Floria M, Dascalita P, Stoica A, Adascalitei P, Sorodoc V, et al. Anemia in heart failure - from guidelines to controversies and challenges. *Anatol J Cardiol.* 2018;20(1):52-9.
- Xia H, Shen H, Cha W, Lu Q. The prognostic significance of anemia in patients with heart failure: A meta-analysis of studies from the last decade. *Front Cardiovasc Med.* 2021;8:632318.
- Segura-Saldaña P, Álvarez-Vargas M, Nieto-Gutiérrez W, Pariona-Javier M, Morán-Mariños C. Producción científica en insuficiencia

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- cardiaca en Perú: un estudio bibliométrico. Arch Cardiol Méx. 2022;92(4):476-83.
22. Rivilla L, Lorente T, Molinero M, García-Erce JA. Anciano y anemia: revisión crítica de su definición y prevalencia. Rev Esp Geriatr Gerontol. 2019;54(4):189-94.
  23. Bermúdez G, Barrientos E, Guarán HA, Hernández B, Pablo B, Andrés S. Proceso de atención de enfermería a paciente con insuficiencia cardiaca congestiva descompensada. Rev Sanit Investig. 2021;2(5):14.
  24. Abebe TB, Gebreyohannes EA, Bhagavathula AS, Tefera YG, Abegaz TM. Anemia in severe heart failure patients: does it predict prognosis? BMC Cardiovasc Disord. 2017;17(1):248.
  25. Ikama MS, Nsitou BM, Kocko I, Mongo NS, Kimbally-Kaky G, Nkoua JL. Prevalence of anaemia among patients with heart failure at the Brazzaville University Hospital. Cardiovasc J Afr. 2015;26(3):140-2.
  26. Cleland JGF, Zhang J, Pellicori P, Dicken B, Dierckx R, Shoaib A, et al. Prevalence and outcomes of anemia and hematinic deficiencies in patients with chronic heart failure. JAMA Cardiol. 2016;1(5):539-47.
  27. Wouters HJCM, van der Klauw MM, de Witte T, Stauder R, Swinkels DW, Wolffenbuttel BHR, et al. Association of anemia with health-related quality of life and survival: a large population-based cohort study. Haematologica. 2019;104(3):468-76.
  28. Casas CR, Indacochea S, Reyes MA. Anemia como factor pronóstico de mortalidad en pacientes con insuficiencia cardiaca en el hospital nacional Edgardo Rebagliati Martins durante enero 2014 a diciembre 2017 [Internet] [Undergraduate thesis]. [Lima]: Universidad Ricardo Palma; 2019. Available from: <https://repositorio.urp.edu.pe/handle/20.500.14138/1989>
  29. Armas CD, Aguilar W, Gutiérrez W. Asociación entre anemia y mortalidad cardiovascular a los 30 días del ingreso en pacientes admitidos en emergencia por insuficiencia cardiaca descompensada [Internet] [Undergraduate thesis]. [Trujillo]: Universidad Nacional de Trujillo; 2017. Available from: <http://dspace.unitru.edu.pe/handle/UNITRU/9362>
  30. Romero JR, Rios JJ. Anemia como factor de riesgo de mortalidad en pacientes hospitalizados con insuficiencia cardiaca [Internet] [Undergraduate thesis]. [Trujillo]: Universidad Nacional de Trujillo; 2017. Available from: <http://dspace.unitru.edu.pe/handle/UNITRU/9615>

**Corresponding author:**

Alberto Guevara Tirado

Address: Calle Doña Delmira manzana E lote 4, Urbanización Los Rosales, Santiago de Surco. Lima, Perú.

Telephone: +51 978 459 469

E-mail: [albertoguevara1986@gmail.com](mailto:albertoguevara1986@gmail.com)

Reception date: February 20, 2023

Evaluation date: March 21, 2023

Approval date: April 11, 2023

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**ORCID iD**

Alberto Guevara Tirado

 <https://orcid.org/0000-0001-7536-7884>