Probability of anemia in pre-diabetics and diabetics: analytical study carried out in a medical center in Villa El Salvador, Lima–Peru

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Abstract

Introduction: The World Health Organization estimates that 2 billion people suffer from anemia, while pre-diabetes and diabetes affect approximately 352 and 460 million people, respectively. Anemia is a frequent complication in diabetes mellitus (DM).

Objective: To evaluate the association and probability of hemoglobin alterations in pre-diabetics and diabetics.

Methodology: Descriptive, retrospective and cross-sectional study, the population was 1103 patients (211 prediabetics, 223 diabetics and 669 normoglycemic), the sample was the total population that met the inclusion and exclusion criteria: normoglycemic and prediabetic adults without the presence of acute or chronic disease at the time of examination. The association between variables was performed using the chi-square test and the probability was determined by the Odds Ratio test.

Results: Pre-diabetic women had a 1.72 higher probability of anemia than non-diabetic women. Pre-diabetic men had 2.80 higher odds of anemia than non-diabetic men. Diabetic women were 2.37 times more likely to have anemia, while diabetic men were 4.41 times more likely than non-diabetic men to have anemia.

Conclusions: Pre-diabetic patients are more likely to have anemia than non-diabetics. It is possible that persistent hyperglycemia in pre-diabetics is associated with changes in the concentration of this hemoprotein years before the development of diabetes by similar mechanisms, but in an incipient form.

Keywords: Anemia; Hyperglycemia; Odds Ratio; Adult; Diabetes Mellitus

Resumen

Introducción: la organización mundial de la salud estima que 2000 millones de personas padecen anemia, mientras que la pre-diabetes y la diabetes afectan aproximadamente a 352 y 460 millones de personas, respectivamente. La anemia es una complicación frecuente en la diabetes mellitus (DM).

Objetivo: evaluar la asociación y probabilidad de alteraciones de la hemoglobina en pre-diabéticos y diabéticos.

Metodología: estudio descriptivo, retorspectivo y transversal, la población fue de 1103 pacientes (211 prediabéticos, 223 diabéticos y 669 normoglucémicos), la muestra fue el total de la población que cumplió con los criterios de inclusión y exclusión: adultos normoglucémicos y pre-diabéticos sin presencia de enfermedad aguda o crónica al momento del examen. La asociación entre variables se realizó por medio de la prueba de chi-cuadrado y la probabilidad fue determinada por la prueba de Odds Ratio.

Resultados: las mujeres pre-diabéticas tuvieron una probabilidad 1.72 mayor de anemia que mujeres no diabéticas. Los hombres pre-diabéticos tuvieron una probabilidad 2.80 veces mayor de anemia que los no diabéticos. Las mujeres diabéticas tuvieron una probabilidad 2,37 más alta de tener anemia, mientras que los hombres diabéticos tuvieron una probabilidad 4,41 veces más alta que lo hombres no diabéticos de padecer anemia.

Conclusiones: pacientes pre-diabéticos tienen mayor probabilidad de anemia que en no diabéticos. Es posible que la hiperglucemia persistente en pre-diabéticos se asocie a cambios en la concentración de esta hemoproteína años antes del desarrollo de diabetes por mecanismos similares, pero de forma incipiente.

Palabras clave: anemia, hiperglucemia, oportunidad relativa, adulto, diabetes mellitus.

Introduction

Anemia affects approximately 2 billion people worldwide (1), while diabetes affects 460 million and pre-diabetes 352 million (2). These diseases have multiple causes, including nutritional deficiencies, inadequate eating habits, sedentary lifestyle, diseases in related organs (myelodysplasia, hypothyroidism, etc.) (3), so the study and understanding of these diseases are relevant for the improvement of quality of life and reduction of morbidity and mortality worldwide.

Anemia is a frequent complication found in diabetics, especially in those with a prolonged period of illness due to microangiopathic complications on the kidneys, with the consequent lower expression of erythropoietin (4). However, it has been found that anemia is prevalent in diabetics with few years of disease, theorizing that hyperglycemia generates a hyperglycemic state, causing fibrocyte changes and interstitial damage that affects the synthesis of erythropoietin, in addition, chronic hyperglycemia would have direct cytotoxic effects on erythrocyte precursor cells in the bone marrow (5).

Changes in serum hemoglobin in diabetics are currently explored and explained in numerous studies such as meta-analyses (6). However, in pre-diabetes, a condition that is a risk factor prior to the development of diabetes mellitus (DM), there could be changes in hemoglobin concentration that are related to persistent elevation of plasma glucose, so the objective of this research was to evaluate the association and probability of anemia in pre-diabetics. The results allow us to contemplate the possibility that alterations in the altered hemoglobin may be an indicator of poor glycemic control in pre-diabetics, and potentially a predictor of the development of DM.

Methodology

Study design and population

Observational, analytical, cross-sectional study using data from medical records of consultations and preventive-promotional health campaigns in normoglycemic and pre-diabetic patients. The study was conducted from June 2021 to December 2022 in a general medicine and physical therapy polyclinic in the district of Villa el Salvador, Lima, Peru. The sampling was non-probabilistic by convenience and included all patients who met the inclusion requirements during the study period. We obtained 1103 of whom 211 were pre-diabetic, 223 were diabetic and 669 had normal glucose. Inclusion criteria were adult patients of both genders who attended prevention evaluations and with normal basal glucose levels (70 to 99 mg/dl) and pre-diabetic patients with altered basal glucose (100 to 125 mg/dl) and diabetes with glucose equal to or greater than 126 mg/dl and clinical signs and symptoms of the disease. Exclusion criteria were patients who attended check-ups for acute or chronic diseases of old or recent diagnosis.

Variables and measurements

Qualitative variables were gender (male, female), age (one group aged 18-44 years and another group aged 45 years or older), blood glucose levels

(normal, pre-diabetes), hemoglobin (normal, anemia). The determination of normal and pre-diabetes glucose was based on the criteria of the American Diabetes Association (ADA) (7) and the determination of hemoglobin levels was based on the recommendation of the World Health Organization (minimum 13 g/L in men and 12 g/L in women) (8). We proceeded to collect and select the data from the clinical histories resulting from the preventive-promotional health campaigns developed from June 2021 to December 2022, saving and ordering this information in the statistical software Excel 2016 to subsequently perform the statistical analysis with the SPSS statistics 25 program.

Statistical analysis

The variables were dichotomized in 2 x 2 tables. Regarding the analytical statistical analysis, the chi-square test was performed to determine if there is an association, as well as the Odds Ratio for the calculation of probabilities. An alpha value equal to 0.05 was considered as the cut-off point for statistical significance.

Ethical considerations

The ethics committee of the polyclinic approved the research (registration number CMD2021-16). The data were coded in an anonymous database, which only included quantifiable data from medical records, and informed consent was not required. Only the investigator had access to the information. The study complied with the ethical standards of the Declaration of Helsinki.

Results

The total number of patients studied was 880, most of them female (n=595). There were 139 pre-diabetic women and 72 pre-diabetic men. Regarding hemoglobin, 93 pre-diabetic women and 42 pre-diabetic men were found with hemoglobin compatible with anemia (Table 1).

Table 1. Table of frequencies in the studied population

			Hemoglobin		Total
			Anemia	Normal	
Female	Blood	Pre-diabetes	93	46	139
		Normal	246	210	456
	Total		**339**	**256**	**595**
Male	Glucemia	Pre-diabetes	42	30	72
		Normal	71	142	213
	Total		**113**	**172**	**285**
Total	Sugar	Pre-diabetes	135	76	211
		Normal	317	352	669
	Total		**452**	**428**	**880**

Source: Own elaboration

After performing the Pearson's chi-square test, a statistical association was found in all variables with a statistical significance level of less than 0.05, both in women (p= 0.007), in men (p=0.001), as well as when analyzed in total (p=0.005). The Odds Ratio (OR) is a test that evaluates the probability of occurrence of an event or disease, in this sense, there was an increase in the probability of developing anemia in female diabetic patients (OR=1.72, CI: 1. 15-2.57) and male (OR=2.8, CI: 1.61-4.84) compared to non-diabetic patients of the same sex, as well as in the total of both genders (OR=1.97, CI: 1.43-2.71), observing that the risk was higher in men (Table 2).

Table 2. Association and odds ratio between pre-diabetes and anemia

	N	OR	IC (95%)	p
Females	595	1.72	1.15-2.57	0.007
Males	285	2.80	1.61-4.84	0.001
Total	**211**	**1.97**	**1.43-2.71**	**0.005**

OR: Odds Ratio. P<0,05 - Source: Own elaboration

Another test was performed to evaluate the association and odds ratio, where the pre-diabetic population was replaced by 223 diabetic patients with a disease duration equal to or greater than 6 months and under treatment, finding an association between all the variables studied and a higher probability of anemia than when the comparative study was performed between pre-diabetics and normoglycemic (Table 3)

Table 3. Association and odds ratio between diabetes and anemia

	N	OR	IC 95%	p
Females	145	2.37	1.57-3.58	0.004
Males	78	4.41	2.51-7.73	0.005
Total	**223**	**2.89**	**2.07-4.03**	**0.012**

OR: Odds Ratio. P<0,05 - Source: Own elaboration

Discussion

Pre-diabetic patients of both genders were found to be more likely to have anemia than those with normal glucose. Erez et al. (9), in a study on the prevalence of anemia in diabetics and pre-diabetics, found a significant prevalence of anemia not related to renal failure in both diabetics and non-diabetics with normal renal function.

However, after searching for other antecedents related to this research, no other similar bibliographic reference was found, being most of the studies related to diabetic patients, therefore, the results obtained try to be explained from the effects of the physiopathology of chronic hyperglycemia in diabetics: glucose homeostasis is maintained by a balance of glyco-regulatory hormones (insulin, glucagon, cortisol, catecholamines, growth hormone) (10), hyperglycemia generates an excess of counter-regulatory hormones, which generates an increase in lipolysis and proteolysis (11), likewise, hyperglycemia generates osmotic diuresis affecting glomerular filtration (12). In turn, persistent hyperglycemia is inherent to the formation of a greater amount of reactive oxygen species due to the high enzymatic interaction with different macromolecules such as lipids and proteins, leading to an inflammatory state characterized by the increase of pro-inflammatory cytokines and oxidative stress in the kidney, resulting in damage to the renal interstitium and peritubular fibrosis (13), affecting the production of erythropoietin; in turn, the increase of free radicals and the release of cytosines affect the hematopoietic precursor cells located in the bone marrow, affecting hematopoiesis (14). It is feasible that hyperglycemia in pre-diabetics acts in a similar way and manifests itself in an incipient form in this group of patients, a situation that differs in diabetic patients where the association and probability of anemia is greater than in the target group of this research.

The limitations of the study were methodological, although there was a sample of 880 participants, the sampling technique was not randomized, but a convenience sampling. Also, although patients with acute or chronic

diseases were excluded, no tests were performed to diagnose hidden disea-
ses using serological tests, tumor markers or imaging tests, due to the high
costs that would increase the expenses of this research, only the patient's
express health manifestation and the physical examination performed du-
ring preventive health campaigns were used to meet the inclusion and ex-
clusion criteria.

Conclusions

The present study conducted in a polyclinic with 880 patients demons-
trates that pre-diabetic patients have a higher risk of anemia than apparently
healthy non-diabetic patients. This result, in addition to the statistical asso-
ciation found, could suggest considering hemoglobin levels in pre-diabetics
as a possible risk factor or subsequent progression to the development of
diabetes mellitus (DM)).

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References

1. Safiri S, Kolahi A-A, Noori M, Nejadghaderi SA, Karamzad N, Bragazzi NL, et al. Burden
    of anemia and its underlying causes in 204 countries and territories, 1990-2019: results
    from the Global Burden of Disease Study 2019. J Hematol Oncol [Internet]. 2021[citado 5
    de diciembre de 2022];14(1):185. Disponible en: http://dx.doi.org/10.1186/s13045-021-
    01202-2

2. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes melli-
    tus and its complications. Nat Rev Endocrinol [Internet]. 2018 [citado 5 de diciembre de
    2022];14(2):88–98. Disponible en: https://pubmed.ncbi.nlm.nih.gov/29219149/

3. Taderegew MM, Gebremariam T, Tareke AA, Woldeamanuel GG. Anemia and its associated
    factors among type 2 diabetes mellitus patients attending Debre Berhan Referral Hospital,
    North-East Ethiopia: A cross-sectional study. J Blood Med [Internet]. 2020 [citado 5 de
    diciembre de 2022];11:47–58. Disponible en: http://dx.doi.org/10.2147/JBM.S243234

4. Mokgalaboni K, Phoswa WN. Cross-link between type 2 diabetes mellitus and iron defi-
    ciency anemia. A mini-review. Clinical Nutrition Open Science [Internet]. 2022 [citado 5 de
    diciembre de 2022];45:57–71. Disponible en: https://www.clinicalnutritionopenscience.
    com/article/S2667-2685(22)00047-X/fulltext

5. Cassidy FC, Shortiss C, Murphy CG, Kearns SR, Curtin W, De Buitléir C, et al. Impact of
    type 2 diabetes mellitus on human bone marrow stromal cell number and phenotypic
    characteristics. Int J Mol Sci [Internet]. 2020 [citado 5 de diciembre de 2022];21(7):2476.
    Disponible en: https://www.mdpi.com/1422-0067/21/7/2476

6. Atlaw D, Tariku Z. Magnitude and factors associated with anemia among diabetic patients
    in Ethiopia: A systematic review and meta-analysis. SAGE Open Med [Internet]. 2021[cita-
    do 5 de diciembre de 2022];9. doi:10.1177/20503121211031126

7. Diabetes standards of care 2022 [Internet]. Guideline Central. 2021 [citado 5 de diciembre
    de 2022]. Disponible en: https://www.guidelinecentral.com/guideline/14119/

8. Akbarpour E, Paridar Y, Mohammadi Z, Mard A, Danehchin L, Abolnezhadian F, et al. Anemia prevalence, severity, types, and correlates among adult women and men in a multiethnic Iranian population: the Khuzestan Comprehensive Health Study (KCHS). BMC Public Health [Internet]. 2022; citado 5 de diciembre de 2022]22(1):168. Disponible en: http://dx.doi.org/10.1186/s12889-022-12512-6

9. Erez D, Shefler C, Roitman E, Levy S, Dovrish Z, Ellis M, et al. Anemia in patients with diabetes and prediabetes with normal kidney function: Prevalence and clinical outcomes. Endocr Pract [Internet]. 2022 citado 5 de diciembre de 2022];28(2):129–34. Disponible en: https://www.sciencedirect.com/science/article/pii/S1530891X21012908

10. Fujikawa T. Central regulation of glucose metabolism in an insulin-dependent and -independent manner. J Neuroendocrinol [Internet]. 2021 citado 5 de diciembre de 2022];33(4):e12941. Disponible en: http://dx.doi.org/10.1111/jne.12941

11. Zhao J, Wu Y, Rong X, Zheng C, Guo J. Anti-lipolysis induced by insulin in diverse pathophysiologic conditions of adipose tissue. Diabetes Metab Syndr Obes [Internet]. 2020 [citado 5 de diciembre de 2022];13:1575–85. Disponible en: https://www.dovepress.com/anti-lipolysis-induced-by-insulin-in-diverse-pathophysiologic-conditio-peer-reviewed-fulltext-article-DMSO

12. Weil EJ, Kobes S, Jones LI, Hanson RL. Glycemia affects glomerular filtration rate in people with type 2 diabetes. BMC Nephrol [Internet]. 2019;20(1):397. Disponible en: http://dx.doi.org/10.1186/s12882-019-1584-7

13. Zeni L, Norden AGW, Cancarini G, Unwin RJ. A more tubulocentric view of diabetic kidney disease. J Nephrol [Internet]. 2017;30(6):701–17. Disponible en: http://dx.doi.org/10.1007/s40620-017-0423-9

14. Santopaolo M, Gu Y, Spinetti G, Madeddu P. Bone marrow fat: friend or foe in people with diabetes mellitus? Clin Sci (Lond) [Internet]. 2020 [citado 5 de diciembre de 2022];134(8):1031–48. Disponible en: https://portlandpress.com/clinsci/article-abstract/134/8/1031/222769/Bone-marrow-fat-friend-or-foe-in-people-with?redirectedFrom=fulltext