Progress in Nutrition 2022; Vol. 24, N. 3: e2022109 DOI: 10.23751/pn.v24i4.12639

Original article

Incidence of obesity and anemia in the diagnosis of breast cancer

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Abstract. Obesity (Ob) and anemia are common pathologies associated with a poor prognosis during breast cancer (BC) treatment. However, there are not enough data on the presence of these pathologies at the time of diagnosis, resulting in a late medical-nutritional intervention, which entails a wide variety of complications that affect the quality of life and prognosis of patients. This study analyzed the presence of Ob and anemia retrospectively in 715 women who were diagnosed with BC. The mean value for the body mass index (BMI) was 29.12kg/m^2 while the highest prevalence in the analysis by age groups was for overweight and Ob; age and BMI showed a positive correlation. 15.43% of the women presented anemia and only a negative correlation trend was observed between hemoglobin values and BMI. The results showed that 7 out of 10 women are overweight and 1 in 6 is anemic, the highest prevalence of anemia was in the overweight group.

Key words: obesity, anemia, breast cancer

Introduction

Breast cancer (BC) is the most common tumor among women worldwide and the first cause of mortality in this group, which makes it a public health problem with an estimated annual incidence of 1.7 million cases and a mortality of 522,000. The Pan American Health Organization estimates for the year 2030 an increase of 60% in diagnoses for this pathology in Latin America. In Mexico, its incidence and mortality have increased in the last three decades (1,2)

Approximately 20% of women diagnosed with BC are older than 50 years (3) and 6.6% are 40 years, in the latter the pathology is usually more aggressive (4,5). Among the risk factors for developing BC are: lower age at menarche, first pregnancy after 30 years, nulliparity, age, use of oral contraceptives, use of hormonal therapy, alcohol consumption, early or late menopause onset, dense breast tissue, hereditary history of breast disease, and postmenopausal obesity (Ob) (4,6,7).

Excess weight is now pandemic and has replaced tobacco as the main lifestyle-related risk factor for premature death. There is enough evidence of a causal link between Ob and the development of cancer. Visceral adipose tissue (VAT) dysfunction in the context of obesity underlies insulin resistance and chronic inflammation, which can lead to the development and progression of BC, with low-grade chronic inflammation becoming an additional stimulus for tumor growth (1,4,8,9), favoring the development of metabolic syndrome, diabetes and cardiovascular events, the latter being the main cause of mortality in women with early-stage BC. Additionally, Ob increases complications, decreases the effectiveness of treatment and increases the risk of local recurrence (5,9,10).

The relationship between overweight/obesity, breast cancer and general risk seems to depend largely

on menopausal status, since obesity is negatively associated with the risk of BC (particularly in postmenopausal women) and with the prognosis of BC. The interrelated molecular mechanisms between Ob and BC could be involved in the pathogenesis in postmenopausal women, with increased levels of endogenous estrogens derived from the excessive expression of aromatase in adipose tissue, overexpression of pro-inflammatory cytokines, resistance to insulin, hyperactivation of the IGF-1 pathways, adipokines, hypercholesterolemia and excess oxidative stress, in addition to the increase in plasma cholesterol that leads to accelerated tumor formation and exacerbates their aggressiveness (1,5–8,11).

Weight gain after BC diagnosis is associated with higher mortality rates. The adverse effects are greater for weight gains equal to or greater than 10% (5,6). The evidence shows that not only Ob is relevant for the development of BC, the distribution of adiposity, tumor characteristics, menopausal status and the use of exogenous hormones are also important (6,7). Increased estrogens and inflammatory mediators have been reported to contribute to the aggressive phenotype of BC in Ob (3). Some studies consider that sarcopenic Ob is related to a worse prognosis in these patients (6).

The worldwide prevalence of anemia ranges from 30 to 90%. This variability is explained by the different definitions of anemia, cancer types and their stages (12–14). Cancer-related anemia (CRA) is a common comorbidity in cancer patients at diagnosis (15) and a significant nearly five-fold increase in the risk of anemia has been reported in patients with newly diagnosed cancer compared with healthy people (16).

CRA does not appear to be a consequence of concurrent antineoplastic therapy, but rather is caused primarily by low-grade chronic inflammation associated with cancer. In addition, it may be related to immune, nutritional, and metabolic components (15). Anemia is also present due to the effect of bleeding associated with the tumor, hemolysis, hypersplenism with hemophagocytosis, bone marrow infiltration, etc., as a consequence of the treatment (chemotherapy, radiotherapy, tyrosine kinase inhibitors, monoclonal antibodies) or the stages of cancer itself (10,14,17–19). Among the most common symptoms of CRA are fatigue, lethargy, dyspnea, anorexia, low cognitive function including difficulty concentrating, and low- energy activity levels (20).

CRA occurs in more than 30% of cancer patients before the initiation of anticancer therapy, while published data from the European Cancer Anaemia Survey (ECAS) suggest that, among non-anemic cancer patients at the start of anti-tumor therapy, the incidence of anemia after chemotherapy is 63%, after chemoradiotherapy 40%, and after radiotherapy 20%. The prevalence seems to increase with age and might differ according to the cancer typology. Indeed, the highest percentage of anemic patients is reported in lung, gynecologic or genitourinary, and gastrointestinal cancers. CRA may accompany the evolution of the cancer, and it is commonly identified in patients at advanced cancer stages. In addition, there is an increasing body of evidence suggesting that anemia is an independent factor adversely affecting antineoplastic treatment efficacy, quality of life and patient survival (15,20).

It has been reported that hemoglobin figures between 11.5 and 10 g/dl, which is considered mild anemia, causes a clear decrease in quality of life (18). A retrospective cohort study in patients with BC and anemia found that hemoglobin levels in the year after cancer treatment correlated with 10-year survival (17), and the risk of death in cancer patients with anemia increased by up to 65% (12).

In cancer patients, with and without anemia, an analysis at 12, 36 and 60 months showed that patients with anemia had an overall survival of 67.2%, 54.0% and 47.0% respectively; while in the group without anemia the overall survival was 82.6%, 68.4% and 62.0%; with significant differences between the global survival curves in both groups ($p < 0.001$). In patients with solid tumors, the overall survival in the anemia cases was 66.6%, 55.0% and 49.0% and in the group without anemia it was 82.6%, 67.4% and 61.2% respectively; with a significant difference also for the global survival curves ($p = 0.002$). These results raise the possibility that anemia can be used as a predictor of survival (12).

Methods

Scope of the research

We conducted an analytical and retrospective study whose objective was to identify the prevalence of

Ob and anemia in women with a recent diagnosis of BC, based on the information included in the clinical record of a High Specialty Hospital, from the period between January 2014 and December 2018.

Data collection

We examined 730 files, excluding those that did not have complete information, leaving 715 files with anthropometric indicators (weight, height and BMI) and hemoglobin, consulted from the hospital MODULAB program. The information was compiled in Excel®.

Statistical analysis

A descriptive statistical analysis was performed for the general data (mean ± SD) also showing the minimum (min) and maximum (max) values, and the inferential analysis used the $\chi 2$ test and ANOVA with post hoc Bonferroni test to compare results between groups. Spearman correlation analysis was applied to identify the relationship between the variables. A p value of 0.05 was considered to be statistically significant. The data were statistically processed with the Statistical Package for the Social Science 23.0 (SPSS) program.

Ethical approval

The study protocol was approved by the Ethics Committee of the hospital with the number CEI-18-19, and the protection of personal data was considered in accordance with the provisions of the general law on the protection of personal data held by obliged subjects.

Results

The present work included 715 records of patients with BC, 5% of the records did not have data regarding hemoglobin levels. Table 1 shows the general data of the participants.

Table 2 shows the comparison of age, anthropometric indicators and hemoglobin between the different age groups, the only variable that did not present significant differences between the groups was hemoglobin.

Table 3 summarizes the nutritional status classified by BMI, both in the general population and in the different age groups, observing significant differences between the groups.

Table 4 shows the correlation analysis, which showed a positive association only between age and BMI, as well as a negative correlation trend between hemoglobin and BMI.

The prevalence of anemia for the general population was 15.43%. Table 5 shows the prevalence of anemia by age groups and BMI, finding only significant differences in the group of older women.

Discussion

Previous reports show that the average age of diagnosis in this population is usually above 50 years (9,21), coinciding with the data obtained in this study

Table 1. Description of variables.

	X (DE)	Minimum	Maximum
N = 715			
Age	53.45 (12.70)	21.00	89.00
Weight (kg)	69.05 (13.30)	37.50	123.00
Height (m)	1.54 (0.07)	1.32	1.78
BMI (kg/m^2)	29.12 (5.40)	17.70	53.50
N = 685			
Hemoglobin (g/dl)	13.29 (1.48)	5.10	17.00

Table 2. Description of variables by age group.

	20 to 40 years X (SD)	41 to 60 years X (SD)	61 to 90 years X (SD)	P
	N= 111	**N =395**	**N= 209**	
Weight (kg)	65.50 (11.80)	70.99 (13.80)	67.25 (12.50)	0.000*
Height (m)	1.55 (0.06)	1.55 (0.07)	1.51 (0.06)	0.000*
BMI (kg/m^2)	27.13 (4.60)	29.5 (0.60)	29.43 (0.37)	0.000*
	N=109	**N=381**	**N=197**	
Hemoglobin (g/dl)	13.29 (1.36)	13.32 (1.49)	13.23 (1.53)	NS

*Variance analysis. *p-value <0.05 Post Hoc Bonferroni test in Weight between group of 20 to 40 years and 41 to 60 years, in Height between 61 to 90 years and 20 to 40 years and 41 to 60 years, for BMI between 20 to 40 years and 41 to 60 years and 61 to 90 years.*

Table 3. Nutritional status according to BMI (N=715).

	General N (%)	20 to 40 years* N (%)	41 to 60 years* N (%)	61 to 90 years* N (%)	P*
Low weight	5(0.70)	2 (1.80)	2(0.51)	1(0.48)	0.003
Healthy weight	154(21.50)	33(29.73)	77(19.49)	44(21.05)	
Overweight	267(37.30)	51(45.95)	144(36.46)	72(34.45)	
Obesity	289(40.40)	25(22.52)	172(43.54)	92(44.01)	

**Chi-square*

Table 4. Correlation analysis among interest variables.

	Age	Weight (kg)	BMI (kg/m^2)	Hemoglobin (g/dl)
Age	-	-0.019	0.120*	-0.023
Weight (kg)	-0.019	-	0.882*	0.025
BMI (kg/m^2)	0.120*	0.882*	-	0.012
Hemoglobin (g/dl)	-0.023	0.025	0.012	-

* The correlation is significant at the 0.01 level

(53.43 years), observing that majority of women had more 40 years old (84.5%), in agreement with the findings reported by Lee et al. (87.1%) (21).

There is enough evidence showing the relationship between Ob and the development of various types of cancer, including BC. Different preclinical and clinical data have provided evidence indicating that obesity may worsen the incidence, the severity, and the mortality of BC (11,22). This relationship between Ob and BC is stronger in women in the postmenopausal women, mainly due to the increase in fat mass that occurs as a compensatory mechanism for estrogen production (7–9), since fat is a metabolically active tissue with elevated levels of the enzyme aromatase that can convert androgens to estrogens (7,10). In the present study, 8 out of 10 women were overweight, which demonstrate the close relationship between Ob and the development of BC, in addition to the fact that Ob increases the risk of recurrence by 12.2% in the 10 years after diagnosis (5), and that being overweight (25-29.9 kg / m2) and Ob (≥ 30 kg / m2) increase the risk of mortality associated with BC [Relative Risk 1.11 (1.07-1.16) for overweight and 1.35 (1.34 -1.47) for Ob (6), in this study, the average BMI value was 29.12 kg / m^2, which places them at higher risk and requires early nutritional care to prevent additional complications.

Table 5. Prevalence of anemia by age group and BMI (N=687).

	Low weight N (%)	Healthy weight N (%)	Overweight N (%)	Obesity N (%)	P
20 to 40 years					
No anemia	3(0.43)	24(3.49)	41(5.96)	25(3.63)	NS
Mild anemia	0(0.00)	2(0.29)	5(0.72)	3(0.43)	
Moderate anemia	0(0.00)	4(0.58)	1(0.14)	1(0.14)	
Severe anemia	0(0.00)	0(0.00)	0(0.00)	0(0.00)	
41 to 60 years					
No anemia	7(1.02)	53(7.74)	136(19.79)	131(19.06)	NS
Mild anemia	0(0.00)	7(1.02)	13(1.89)	11(1.60)	
Moderate anemia	0(0.00)	5(0.72)	8(1.16)	8(1.16)	
Severe anemia	0(0.00)	0(0.00)	2(0.72)	0(0.00)	
61 to 90 years					
No anemia	5(0.72)	34(4.94)	47(6.84)	75(10.91)	0.046
Mild anemia	0(0.00)	5(0.72)	8(1.16)	6(0.87)	
Moderate anemia	0(0.00)	8(1.16)	7(1.02)	1(0.14)	
Severe anemia	0(0.00)	1(0.14)	0(0.00)	0(0.00)	

**Chi-square*

Considering that age has effects both on changes in body composition and on the development of excess weight, for the analysis of results in this study three age groups were formed: 1) 20 to 40 years, 2) 41 to 60 years and 3) 61 to 90 years, observing statistically significant differences between them in the indicators of height, weight and BMI (p = 0.000). A significant difference in height was found in the older age group, which may be explained by the fact that some women decrease in height as they age. A significant difference was found between the weight of group 1 and 2. It is relevant to point out that women in the perimenopausal stage (age group 41 to 60 years) presented greater excess weight, which is attributable to the hormonal changes characteristic of this stage (9), as detailed above, and which possibly influenced in BC development (5,10).

When we compared the distribution of the different nutritional states according to BMI (low weight, healthy weight, overweight and Ob) it showed statistically significant differences (p = 0.003) between group 1 compared to groups 2 and 3. A higher prevalence of overweight was also observed for the group of women between 20 and 40 years old (45.95%), while the highest prevalence of Ob was found in women older than 41 years, with a percentage close to 45%. This trend was demonstrated by correlation analysis, which showed a positive association between age and BMI.

It is important to note that weight and BMI are the most commonly used measures to assess the patient's condition and often their nutritional status, however, these measures do not assess body composition. Patients may have a critical loss of muscle mass and remain overweight (sarcopenic Ob), they do not necessarily gain or lose fat and muscle proportionally with weight change, so an assessment of body composition should become an indispensable element in the evaluation of these patients (7). This is especially relevant for women with BC older than 40 years, who have a higher prevalence of sarcopenic Ob, since sarcopenic Ob, generating a profound impact on treatment tolerance, efficacy, progression and survival (21).

Reports refer that anemia in women of reproductive age living in low- and middle-income countries ranges between 29 and 38% (12,23). In Mexico the latest data from the National Survey of Nutrition and Health (ENSANUT) 100k, carried out with a population of low socioeconomic status, report a prevalence of 34.3% in women between 12 and 49 years of age

(23,24). Although anemia is another risk factor that adds to the vulnerability of this group of women, there are few studies that report the presence of anemia at the time of cancer diagnosis, including Kenar et al. (16) found 49.7% while before starting treatment Natalucci et al. (15) reported 30% and Gilreath et al. (25) 39% according to data from the European Cancer Anaemia Survey (ECAS 2004), while other studies report a range between 30 and 90%, without discriminating between sexes or different types and stages of cancer (12), and 2 to 78% for solid tumors (17), as for BC, Paitan et al. (13) refer a prevalence of 26.3%. These percentages are higher than the 15.4% found in this study, we consider that these differences can be attributed to the different moments in which it was analyzed (progression of the disease, treatment cycles, disease stage, etc.).

In the present investigation, the average hemoglobin value does not show the presence of anemia (13.29 gr / dl ± 1.4 SD), this agrees with what was found by Lee et al. (12), however, it is important to consider the values in the range that oscillate between 5.10gr / dl - 17gr / dl, showing how some women are in a severe degree of anemia and require early nutritional medical intervention. We observed a higher prevalence of anemia in the age group 41-60 years, but statistically significant differences between the degree of anemia and BMI were only observed in the age group 61-90 years; however, it is noteworthy that in the low weight group no cases of anemia were identified while in the group of women with Ob the prevalence was 4.34%.

It is important to point out that anemia is a condition that deserves special attention, since its appearance is due to multiple conditions. A mechanism has been identified that explains its presence in individuals with diseases that cause prolonged immune activation and consequently chronic inflammation, characteristics present in women with BC and Ob, where changes in the production of cytokines can lead to an alteration in the production of erythropoietin and in the response of erythroid precursors such as hepcidin, producing what is known as inflammatory anemia or anemia of chronic diseases (26,27).

We consider that the important contribution of this study is the information related to the BMI and anemia data at the time of diagnosis, since most of the data reported in most of the studies focus on the stages of treatment. It is important to highlight the importance of individualized analysis that considers the evaluation of body composition and not only variables of weight, height and BMI with the aim of identifying Ob or sarcopenic Ob since the amount and location of the fat mass has important implications in the evolution and prognosis of these patients.

Limitations

The nature of the retrospective design makes it difficult to rectify or modify the data, and some files did not contain complete information. The data collection was in a single hospital center, which refers only to local data.

Conclusion

Our results show that 7 out of 10 women were overweight or Ob, present mainly in older women. Anemia was present in all age groups, but not in all BMI classifications, finding statistically significant differences between the degree of anemia and BMI only in older women. Considering that anemia and BMI are modifiable conditions and with important effects on the prognosis of the disease, it is necessary to give importance to timely care from the moment of diagnosis, with special attention to older women.

It is recommended to consider an evaluation that includes important variables such as fat mass and fat-free mass, due to the implications that this represents in the quality of life and prognosis of women with BC, comprehensively addressing the BC-Ob -anemia triad.

Funding: This research received no external funding.

Conflict of interest: The authors who work in the hospital where the study was carried out declare conflict of interest due the institutional relationship, the rest of the researchers do not present any conflict of interest.

References

1. García-Estévez L, Cortés J, Pérez S, Calvo I, Gallegos I, Moreno-Bueno G. Obesity and Breast Cancer: A Paradoxical and Controversial Relationship Influenced by Menopausal Status. Front Oncol. 2021;11:705911.
2. Cárdenas-Sánchez J, Erazo-Valle-Solís AA, Arce-Salinas C, et al. Consenso Mexicano sobre diagnóstico y tratamiento del cáncer mamario. Octava revisión. Colima 2019. Gac Mex Oncol. 2019;18(3):141-231.
3. Picon-Ruiz M, Morata-Tarifa C, Valle-Goffin JJ, Friedman ER, Slingerland JM. Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention: Breast Cancer, Inflammation, and Obesity. CA Cancer J Clin. 2017;67(5):378- 97.
4. Laudisio D, Muscogiuri G, Barrea L, Savastano S, Colao A. Obesity and breast cancer in premenopausal women: Current evidence and future perspectives. Eur J Obstet Gynecol Reprod Biol. 2018;230:217-21.
5. Engin A. Obesity-associated Breast Cancer: Analysis of risk factors. Adv Exp Med Biol. 2017;960:571-606.
6. Fortner RT, Katzke V, Kühn T, Kaaks R. Obesity and Breast Cancer. Recent Results Cancer Res, 2016;208:43-65.
7. Park JW, Han K, Shin DW, et al. Obesity and breast cancer risk for pre- and postmenopausal women among over 6 million Korean women. Breast Cancer Res Treat. 2021;185(2):495-506.
8. Iwase T, Wang X, Shrimanker TV, Kolonin MG, Ueno NT. Body composition and breast cancer risk and treatment: mechanisms and impact. Breast Cancer Res Treat. 2021;186(2):273-83.
9. Bhardwaj P, Au CC, Benito-Martin A, et al. Estrogens and breast cancer: Mechanisms involved in obesity-related development, growth and progression. J Steroid Biochem Mol Biol. 2019;189:161-70.
10. Davis MP, Panikkar R. Sarcopenia associated with chemotherapy and targeted agents for cancer therapy. Ann Palliat Med. 2019;8(1):86-101.
11. Lohmann AE, Goodwin PJ. Obesity and Breast Cancer: Expanding the Hypothesis Space. JNCI J Natl Cancer Inst. 2021;113(2):107-8.
12. Lee CL, Tsai CH, Yeh DC, Lin CS, Li YF, Tzeng HE. Hemoglobin level trajectories in the early treatment period are related with survival outcomes in patients with breast cancer. Oncotarget. 2017;8(1):1569-79.
13. Paitan V, Alcarraz C, Leonardo A, et al. Anemia como factor pronóstico en pacientes con cáncer. Rev Peru Med Exp Salud Pública. 2018;35(2):250.
14. Chen B, Dai D, Tang H, et al. Pretreatment Hematocrit Is Superior to Hemoglobin as a Prognostic Factor for Triple Negative Breast Cancer. Ahmad A, editor. PLoS One. 2016;11(11):e0165133.
15. Natalucci V, Virgili E, Calcagnoli F, et al. Cancer Related Anemia: An Integrated Multitarget Approach and Lifestyle Interventions. Nutrients. 2021;13(2):482.
16. Kenar G, Köksoy EB, Ürün Y, Utkan G. Prevalence, etiology and risk factors of anemia in patients with newly diagnosed cancer. Support Care Cancer. 2020;28(11):5235- 42.
17. Maccio A, Madeddu C, Gramignano G, et al. The role of inflammation, iron, and nutritional status in cancer-related anemia: results of a large, prospective, observational study. Haematologica. 2015;100(1):124-32.
18. Abiri B, Vafa M. Iron Deficiency and Anemia in Cancer Patients: The Role of Iron Treatment in Anemic Cancer Patients. Nutr Cancer. 2020;72(5):864-72.
19. Abdel-Razeq H, Hashem H. Recent update in the pathogenesis and treatment of chemotherapy and cancer induced anemia. Crit Rev Oncol Hematol. 2020;145:102837.
20. Danzinger S, Fügerl A, Pfeifer C, Bernathova M, Tendl-Schulz K, Seifert M. Anemia and Response to Neoadjuvant Chemotherapy in Breast Cancer Patients. Cancer Invest. 2021;39(6-7):457-65.
21. Lee K, Kruper L. Dieli-Conwright CM, Mortimer JE. The Impact of Obesity on Breast Cancer Diagnosis and Treatment. Curr Oncol Rep. 2019;21(5): 1-6.
22. Barone I, Giordano C, Bonofiglio D, Andò S, Catalano S. The weight of obesity in breast cancer progression and metastasis: Clinical and molecular perspectives. Semin Cancer Biol. 2020;60:274-84.
23. Shamah-Levy T, Mejía-Rodríguez F, Méndez Gómez-Humarán I, De la Cruz- Góngora V, Mundo-Rosas V, Villalpando-Hernández S. Tendencia en la prevalencia de anemia entre mujeres mexicanas en edad reproductiva 2006-2016. Ensanut MC 2016. Salud Pública México. 2018;60(3):301-8.
24. Mejía-Rodríguez F, Mundo-Rosas V, Rodríguez-Ramírez S, et al. Alta prevalencia de anemia en mujeres mexicanas en pobreza, Ensanut 100k. Salud Pública México. 2019;61(6, nov-dic):841-51.
25. Gilreath JA, Stenehjem DD, Rodgers GM. Diagnosis and treatment of cancer-related anemia: Diagnosis and treatment of cancer-related anemia. Am J Hematol. 2014;89(2):203- 12.
26. González-Domínguez Á, Visiedo-García FM, Domínguez-Riscart J, González- Domínguez R, Mateos RM, Lechuga-Sancho AM. Iron Metabolism in Obesity and Metabolic Syndrome. Int J Mol Sci. 2020;21(15):1-27.
27. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood. 2019;133(1): 40- 50.

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