Obesity as a Risk Factor and Prognostic Indicator for B-cell Lymphoma: An Umbrella Review

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Abstract: *Introduction*: Obesity constitutes an important risk factor for numerous chronic diseases, including various types of cancer. Epidemiological evidence shows that individuals with elevated body mass index (BMI) present a higher incidence of malignant tumors, including hematological neoplasms like B-cell lymphomas.

Objective: To synthesize and evaluate the available evidence regarding the dual role of obesity both as a risk factor for developing B-cell lymphoma and as a prognostic indicator in patients already diagnosed with this malignancy.

Methodology: This umbrella review followed PRISMA guidelines. A comprehensive search was conducted in PubMed/MEDLINE, Scopus, Embase, Web of Science, and Cochrane databases. Studies were included if they were systematic reviews or meta-analyses examining obesity/BMI as a risk factor or prognostic indicator for B-cell lymphoma, particularly DLBCL. The ROBIS tool was used to assess methodological quality.

Results: Systematic reviews consistently demonstrate that elevated BMI increases the risk of developing DLBCL, with relative risk estimates between 1.11-1.31. Obese individuals have approximately 11-31% greater risk compared to those of normal weight, with stronger associations observed for BMI during early adulthood. For prognosis, while underweight consistently shows negative effects on survival, the impact of overweight and obesity varies. One review identified a protective effect of overweight (BMI 25-29.9 kg/m²) on overall survival (HR=0.86), suggesting an "obesity paradox," while others found neutral effects.

Conclusions: The obesity-lymphoma relationship involves chronic inflammation, adipokine dysregulation, insulin resistance, and altered tumor microenvironment. Clinical recommendations include detailed body composition assessments, personalized nutritional interventions, and adapted physical exercise programs.

Keywords: B-cell lymphoma, DLBCL, obesity, body mass index, adiposity, risk factor, prognosis, overall survival, obesity paradox, chronic inflammation, adipokines, insulin resistance, body composition.

1. INTRODUCTION

Obesity has become a global health problem of epidemic proportions. According to the WHO, in 2022, approximately one in eight individuals worldwide was obese [1]. This condition, defined by excessive accumulation of body fat, constitutes an important risk factor for numerous chronic non-communicable diseases, significantly increasing the likelihood of developing type 2 diabetes, cardiovascular diseases, and various types of cancer. It has been estimated that excess weight contributes to the development of at least thirteen types of cancer in humans [2].

The association between obesity and cancer is supported by abundant epidemiological evidence. Multiple prospective studies have demonstrated that individuals with elevated body mass index (BMI) present a higher incidence of several common malignant tumors and hematological neoplasms [3]. A recent meta-analysis of cohort studies reported that obesity is linked to a significant increase in the risk of non-Hodgkin lymphoma (NHL), as well as an increased risk of leukemia and multiple myeloma, compared to normal weight.

B-cell lymphomas constitute a heterogeneous group of hematological cancers that comprise approximately 85% of all NHL cases in adults [4,5]. The most common subtypes are diffuse large B-cell lymphoma

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(DLBCL) and follicular lymphoma, representing approximately half of all NHL cases. DLBCL is the most frequent type and typically presents with rapid growth, requiring early diagnosis and treatment [6]. Follicular lymphoma usually follows a slower course in its initial stages, although it can become aggressive.

Building on this, various studies have explored whether obesity influences the risk of developing B-cell lymphomas. For example, a meta-analysis of epidemiological studies reported that obese individuals present a higher relative risk of developing DLBCL compared to people of normal weight [7,8]. Furthermore, the influence of obesity might not be limited solely to the onset of lymphomas but could also have important implications for the prognosis of diagnosed patients [9]. Some studies suggest that the obesogenic state may be associated with differences in clinical outcomes and survival of these patients.

Considering the growing evidence in both areas, a comprehensive synthesis through an Umbrella Review is necessary. This methodology will allow for an integral evaluation of the association between obesity and the risk of B-cell lymphoma and its prognostic impact. This will provide a unified framework of the available scientific evidence, which is fundamental for informing public health recommendations and guiding future research at the intersection of obesity and lymphatic cancer.

METHODOLOGY

Design Study

This study will be conducted as an Umbrella Review of previous systematic reviews and meta-analyses that have evaluated obesity as a risk factor and a prognostic indicator in B-cell lymphoma. Following the methodological guidelines for this type of study, the PRISMA statement adapted for these designs will be applied [10].

Search Strategy

To identify systematic reviews and meta-analyses on the association between obesity and B-cell lymphoma—both in terms of risk and prognosis—various international databases will be used: PubMed/MEDLINE, Scopus, Embase, Web of Science, and Cochrane Database of Systematic Reviews. No language restrictions will be imposed; however, in case of a high volume of results in other languages, studies in English and Spanish will be prioritized. To maximize comprehensiveness, gray literature will also be included through Google Scholar, and reference lists of articles identified as relevant will be reviewed.

The search scheme will combine controlled descriptors and uncontrolled key terms. On one hand, it will include terms related to obesity and overweight (for example: "obesity", "overweight", "BMI", "body mass index", "adiposity") and, on the other hand, those linked to B-cell lymphoma (such as "B-cell lymphoma", "non-Hodgkin lymphoma", "diffuse large B-cell lymphoma", "follicular lymphoma", as well as their synonyms in Spanish). These terms will be connected using Boolean operators (AND, OR), and truncations or wildcards (for example, "obes*") will be used to ensure the retrieval of all relevant variants.

Eligibility Criteria

This study will include only systematic reviews and/or meta-analyses that evaluate the relationship between obesity or overweight and the risk of B-cell lymphoma, published from 2013 until the search closing date. For a secondary study to be incorporated, it must meet certain minimum requirements: first, it must have explicitly defined the inclusion criteria for primary studies and described the bibliographic search methodology in a reproducible manner; second, it must have quantitatively or qualitatively evaluated the association between obesity or overweight (measured mainly through body mass index, although indicators of abdominal adiposity may also be considered) and the incidence or risk of B-cell lymphoma, either globally or in specific subtypes (such as diffuse large B-cell lymphoma or follicular lymphoma); third, include studies conducted in adult humans (≥18 years); and, finally, present effect estimates (for example, relative risk, odds ratio, hazard ratio) or, failing that, a narrative synthesis of the relevant findings.

In this review, the terms “BMI” and “obesity” are used to refer to clinical categories based on body mass index, while “adiposity” is used to describe fat tissue quantity or distribution as measured through imaging or other direct methods.

Reviews that do not meet the characteristics of a systematic review will be excluded, for example, narrative reviews that lack a search protocol and defined inclusion criteria, as well as those focused exclusively on neoplasms that do not correspond to B-cell lymphoma or duplicates of the same meta-analysis or review. Likewise, preliminary reports, congress abstracts, letters to the editor, and articles from which

the full text or essential information for analysis cannot be obtained will be discarded. When doubts arise regarding the eligibility of a review, a discussion with a second investigator will be used to reach a consensus. Finally, in the case of articles that include both B-cell lymphoma and other hematological neoplasms, it will be considered eligible only if the results relating to B-cell lymphoma are presented specifically or if the data can be extracted independently.

Data Extraction

Data extraction will be carried out using a structured form designed for this study to ensure uniformity and accuracy in information collection. To begin with, each selected systematic review or meta-analysis will be carefully and independently reviewed by two researchers, who will complete the form by noting the relevant data to answer the questions of this Umbrella Review. The information to be extracted will include both that related to the identification of the article (title, first author, year of publication, journal or source) and that describing the methodology used, such as the databases consulted, the search period, the number of primary studies included, the inclusion and exclusion criteria, and the tool used to evaluate the quality and bias of the studies.

During this review process, special attention will be paid to how each review defines and evaluates obesity or overweight to ensure the comparability of results. This involves recording the anthropometric measure used (for example, body mass index and waist circumference) and the cut-off points used to define obesity. Likewise, the sociodemographic characteristics of the studied populations will be detailed, emphasizing age ranges, sex, and possible comorbidities. In addition, the analytical strategies of each review will be documented, identifying the confounding variables considered, the heterogeneity tests used, and any meta-regression or sensitivity analysis reported.

Regarding quantitative results, measures of association (odds ratio, relative risk, hazard ratio) and their respective confidence intervals will be extracted, and p-values will be related to statistical significance. The pooled effects that contemplate the association between obesity and B-cell lymphoma globally or concerning specific subtypes (for example, diffuse large B-cell lymphoma) will also be recorded. When reviews include a meta-analysis, efforts will be made to obtain heterogeneity data (such as I^2) and the results of tests to detect publication bias (for example, funnel plots and Egger's test).

Risk of Bias

The risk of bias in the included systematic reviews was assessed using the Risk of Bias in Systematic Reviews (ROBIS) tool, which examines essential methodological aspects to determine the quality of each review. Specifically, the assessment focuses on four fundamental dimensions: (1) the definition of eligibility criteria, (2) the identification and selection of primary studies, (3) data collection and the method of assessing their quality, and (4) the synthesis and interpretation of results. Two independent reviewers systematically applied this tool to each eligible review; in case of disagreement, the discrepancy was resolved with the judgment of a third reviewer.

At the end of this process, a global bias judgment was assigned that classifies each review as "low," "high," or "uncertain" level of bias, according to the degree of methodological rigor observed in each of the four domains. This rating provides a comprehensive perspective on the reliability of each review, as it considers both the validity of the bibliographic search and the inclusion of studies, as well as the veracity of the synthesis of their findings.

RESULTS

Eligible Studies

The initial search in electronic databases identified 100 records (Scopus=44, Embase=25, PubMed=16, Web of Science=15), with no additional records identified from other sources. After removing duplicates, 52 unique records were obtained for initial screening. Of these, 42 records were excluded for the following reasons: they did not evaluate BMI/obesity as a risk factor for DLBCL (n=21), methodological designs not eligible for this umbrella review (n=15), and reviews that did not report association measures (n=16). Four additional studies were excluded from the 10 articles assessed in full text because they did not provide specific effect estimates for BMI and DLBCL (n=7) and focused on prognosis rather than risk factors (n=3). Finally, six studies met the inclusion criteria and were included in the qualitative synthesis [7-9,11-13].

BMI as a Risk Factor: Synthesis of Findings

The three systematic reviews analyzed converge on a crucial point [7,8,12]: : there is a positive association between elevated body mass index and the development of DLBCL (Table **1**). This consistency across different methodologies and inclusion criteria

Table 1: Summary Table of Systematic Reviews on Obesity as a Risk or Prognostic Factor for DLBCL

First Author, Year	Type of Review	Main Objective of Review	Population and/or Lymphoma Subtypes Included	Number of primary Studies and Total Sample Size	Exposure or Variable of Interest	Association Measures and Main Results	Main Conclusions of the Review
Castillo *et al*., 2013	Systematic review with meta-analysis	To evaluate the association between obesity and risk of diffuse large B-cell lymphoma	Adults with diffuse large B-cell lymphoma (DLBCL)	16 studies; approximately 7500 cases	Obesity defined as BMI ≥30 kg/m², overweight as BMI 25–29.9 kg/m²	RR=1.14 (95% CI: 1.04-1.24) for overweight; RR=1.29 (95% CI: 1.16-1.43) for obesity	Increased BMI is associated with a higher risk of DLBCL, with a linear relationship between BMI and DLBCL incidence
Wang *et al*., 2021	Systematic review with meta-analysis	To evaluate the effect of BMI on diffuse large B-cell lymphoma prognosis	Patients with diffuse large B-cell lymphoma	12 studies; number of cases not specified	BMI in categories: underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), obesity (≥30.0)	Underweight associated with worse survival (OS: HR=1.97, 95% CI 1.41-2.74); obesity not significantly associated with OS or PFS	Underweight is a risk factor for worse prognosis in DLBCL; obesity showed no clear association
Hidayat *et al*., 2018	Systematic review with meta-analysis	To analyze the relationship between anthropometric factors and risk of non-Hodgkin lymphoma	Patients with non-Hodgkin lymphoma, including DLBCL and other subtypes	22 studies; more than 20,000 NHL cases	BMI, weight and height in early adulthood and current	RR=1.06 (95% CI: 1.03-1.09) per 5 kg/m² increase in BMI; RR=1.11 (95% CI: 1.07-1.16) for BMI in early adulthood	BMI and weight in early adulthood have greater impact on NHL risk than current BMI and weight values
Aleixo *et al*., 2022	Systematic review with meta-analysis	To evaluate the prognostic impact of adiposity in hematological malignancies	Patients with lymphoma, acute myeloid leukemia, and multiple myeloma	7 studies; 665 patients	Visceral and subcutaneous adiposity, evaluated through computed tomography images	HR=2.02 (95% CI: 1.30-3.14) for mortality in low visceral adiposity; HR=2.98 (95% CI: 1.69-5.26) for low subcutaneous adiposity	Patients with low adiposity (subcutaneous or visceral) have worse survival in hematological malignancies
Wang *et al*., 2020	Systematic review with meta-analysis	To evaluate the impact of BMI on survival of patients with diffuse large B-cell lymphoma	Patients with diffuse large B-cell lymphoma	14 studies; 8,753 patients	BMI in categories: underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), obesity (≥30.0)	HR=0.86 (95% CI: 0.78-0.95) for overweight in OS; HR=1.99 (95% CI: 1.45-2.74) for underweight in OS	Overweight is associated with better survival in DLBCL, while underweight is associated with worse survival
Vera-Ponce *et al*., 2024	Revisión sistemática con metanálisis	Determinar la asociación entre linfoma difuso de células B grandes y el IMC	Adultos con linfoma difuso de células B grandes (DLBCL)	13 estudios; periodo de 2002-2013	IMC en categorías: normal, sobrepeso, obesidad, con seguimiento de cohortes	RR=1.31 (IC 95%: 1.07-1.61) para IMC alto en el riesgo de DLBCL	El alto IMC está asociado con mayor riesgo de DLBCL; se requiere más investigación sobre los mecanismos biológicos subyacentes

reinforces the solidity of this relationship. Relative risk estimates vary between 1.11 and 1.31, indicating that obese individuals have approximately 11-31% greater risk of developing DLBCL compared to those of normal weight.

The research by Castillo *et al*. (2014) [7] established a specific meta-analysis for DLBCL for the first time, finding a 29% increase in relative risk in obese individuals. This review included case-control and

cohort studies, providing a broad evidence base that encompassed approximately 7,500 cases of DLBCL.

For their part, Hidayat *et al*. (2018) [12] expanded the analysis to include multiple anthropometric factors, revealing that for each 5 kg/m² increase in BMI, the risk of DLBCL increases by 11%. Significantly, this review provided an additional important observation: BMI during early adulthood (18-21 years) showed a stronger association with the risk of developing non-Hodgkin lymphoma than BMI in late adulthood, suggesting that early exposure to obesity might play a more decisive role in pathogenesis.

The most recent review, conducted by Vera-Ponce *et al*. (2024) [8], applied stricter methodological criteria, including only studies with objective BMI measurements and focusing exclusively on cohort studies. Despite these more rigorous criteria, their results confirm and reinforce previous findings, finding a relative risk of 1.31 for individuals with elevated BMI.

Finally, it is important to highlight the high degree of concordance among the three systematic reviews, with nine primary studies included in all of them (Cerhan 2002, Lim 2007, Britton 2008, Maskarinec 2008, Lu 2009, Pylypchuk 2009, Troy 2010, Kabat 2012, and Nagel 2012), which represents approximately 40.9% of the total unique studies identified. This consistency in primary sources reinforces the solidity of the evidence base upon which the conclusions are built.

BMI AS A PROGNOSTIC FACTOR: SYNTHESIS OF FINDINGS

The impact of BMI on prognosis in patients with DLBCL reveals distinct patterns depending on the BMI category—underweight, overweight, or obesity (Table 4). For context, hazard ratios or relative risks are typically presented with 95% confidence intervals (CI), which indicate the range within which the true effect size is expected to lie with 95% certainty. If the CI does

Table 2: Table of Coincidences of Primary Studies between Systematic Reviews on BMI as a Risk Factor for DLBCL

Study First Author, Year	Castillo *et al*. (2014) [7]	Hidayat *et al*. (2018) [12]	Vera-Ponce *et al*. (2024) [8]
Cerhan *et al*. (2002)	□	□	□
Chang *et al*. (2005)		□	□
Rapp *et al*. (2005)	□		
Lukanova *et al*. (2006)	□		
Samanic *et al*. (2006)	□		
Oh *et al*. (2005)	□		
Engeland *et al*. (2007)	□	□	
Lim *et al*. (2007)	□	□	□
Britton *et al*. (2008)	□	□	□
Maskarinec *et al*. (2008)	□	□	□
Lu *et al*. (2009)	□	□	□
Pylypchuk *et al*. (2009)	□	□	□
Söderberg *et al*. (2009)	□		
Kanda *et al*. (2010)		□	
Troy *et al*. (2010)	□	□	□
Kabat *et al*. (2012)	□	□	□
Nagel *et al*. (2012)	□	□	□
Bertrand *et al*. (2013)		□	□
Patel *et al*. (2013)	□	□	□
Murphy *et al*. (2013)		□	□
Bhaskaran *et al*. (2014)			□
Kabat *et al*. (2014)		□	
MacInnis *et al*. (2005)		□	

not cross 1.0, the result is usually considered statistically significant.

All three systematic reviews consistently report that underweight (BMI <18.5 kg/m²) is associated with worse overall survival. For example, Wang *et al*. (2020) [11] found a nearly twofold increase in mortality risk (HR=1.99, 95% CI: 1.45–2.74), meaning underweight patients had almost twice the risk of death compared to those of normal weight. This negative effect is echoed in Wang *et al*. (2021) [9] and reinforced by Aleixo *et al*. (2022), who showed that low visceral and subcutaneous adiposity, as assessed through imaging, was significantly linked to poorer survival.

The overweight (BMI 25.0–29.9 kg/m²) findings are more heterogeneous. Wang *et al*. (2020) [11] observed a statistically significant protective effect on overall survival (HR=0.86, 95% CI: 0.78–0.95), indicating that overweight patients had a 14% lower risk of death compared to those with normal BMI, suggesting a possible "obesity paradox." However, Wang *et al*. (2021) [9] did not replicate this association (HR=0.93, 95% CI: 0.78–1.11), instead reporting a neutral impact on survival outcomes. Population differences, clinical settings, or methodological variability may influence this inconsistency.

Regarding obesity (BMI ≥30.0 kg/m²), the reviews suggest a generally neutral association with prognosis. Wang *et al*. (2020) [11] found no significant impact on overall survival (HR=1.11, 95% CI: 0.81–1.53), indicating a similar risk of death to normal-weight individuals. This finding was supported by Wang *et al*. (2021) [9] and indirectly by Aleixo *et al*. (2022) [13]. Although Aleixo's review focused on adiposity distribution rather than BMI categories, their results suggest that body composition indicators (e.g., adipopenia) may better predict prognosis than BMI alone.

In summary, while the negative effect of underweight is consistently supported, evidence remains mixed regarding overweight and obesity. This

Table 3: Table of Coincidences of Primary Studies between Systematic Reviews on BMI as a Prognostic Factor in DLBCL

Study First author, year	Wang *et al*., 2021 [9]	Wang *et al*., 2020 [11]	Aleixo *et al*., 2022 [13]
Geyer *et al*., 2010	□	□	□
Jones *et al*., 2010	□	□	□
Carson *et al*., 2012	□	□	□
Han *et al*., 2013	□	□	
Camus *et al*., 2014	□	□	□
Hong *et al*., 2014	□	□	□
Leo *et al*., 2014	□	□	
Sarkozy *et al*., 2014	□	□	
Weiss *et al*., 2014	□	□	
Hwang *et al*., 2015	□	□	□
Shin *et al*., 2016	□	□	□
Zhou *et al*., 2016	□	□	
Bendtsen *et al*., 2017	□	□	□
Boyle *et al*., 2017	□	□	□
Li *et al*., 2017	□		
Kanemasa *et al*., 2018	□	□	□
Burkart *et al*., 2019			□
Coutinho *et al*., 2019	□		
Mörth *et al*., 2019	□		
Chan *et al*., 2016	□		
Jung *et al*., 2021			□
Cunha *et al*., 2021			□

Table 4: Summary of Findings on BMI Categories and Prognosis in Patients with DLBCL

BMI Category	Main Findings	Reviews Supporting the Finding	Interpretation
Underweight	Worse overall survival (OS). HR≈1.97	Wang *et al*. (2020), Wang *et al*. (2021), Aleixo *et al*. (2022)	Consistently negative impact
Overweight	Possible protective effect (HR=0.86), but not consistent across studies	Wang *et al*. (2020) (positive), Wang *et al*. (2021) (neutral)	Evidence of "obesity paradox" not conclusive
Obesity	Neutral or non-significant effect on OS	Wang *et al*. (2020), Wang *et al*. (2021), Aleixo *et al*. (2022)	Body composition may matter more than BMI

underscores the importance of evaluating BMI and body composition in future studies addressing DLBCL prognosis. Also, this protective effect of overweight suggests a possible 'obesity paradox' (a counterintuitive phenomenon in which overweight or mildly obese patients with certain diseases, such as cancer or cardiovascular conditions, appear to have better survival outcomes than those of normal weight). However, this has not been consistently observed.

DISCUSSION

Principal's Findings

The findings of this umbrella review confirm a significant association between obesity and B-cell lymphoma, highlighting both the increased risk of developing DLBCL and its impact on patient prognosis. Although mechanisms such as chronic inflammation, metabolic dysfunction, and hormonal alterations explain much of this relationship, contradictory results persist regarding the effect of overweight and obesity on survival. This variability underscores the importance of considering additional factors such as adipose tissue distribution, overall nutritional status, and present comorbidities, evidencing the need for deeper investigations and a comprehensive clinical approach that includes detailed assessments of body composition, personalized nutritional interventions, and adapted physical exercise programs to optimize both prevention and therapeutic management of these patients.

Biological Implications

Obesity is characterized by low-grade chronic inflammation, resulting from increased secretion of proinflammatory cytokines (such as interleukin-6 and tumor necrosis factor-alpha, TNF-α) by adipose tissue [14]. In addition to mediating a systemic inflammatory response, these cytokines can interfere with cell cycle control mechanisms, facilitating the survival and proliferation of malignant cells. In the case of DLBCL, the persistence of proinflammatory signals creates a microenvironment conducive to tumor growth and evasion of apoptosis.

A second relevant mechanism involves altering signaling pathways regulated by adipokines, especially leptin and adiponectin. Leptin, whose levels increase in obesity, promotes cell proliferation and angiogenesis through pathways such as JAK/STAT and PI3K/AKT. In contrast, adiponectin, which tends to decrease with overweight and obesity, possesses anti-inflammatory and insulin-sensitizing properties; its deficit contributes to a more favorable environment for tumorigenesis and progression of B-cell lymphoma [15].

Obesity is often associated with insulin resistance and elevations in insulin-like growth factor type 1 (IGF-1) production. These molecules promote cell proliferation and reduce apoptosis, two critical processes for lymphoma development. Although much of the evidence on insulin resistance and IGF-1 comes from studies on solid tumors, it is considered that the same hormonal axis may influence the malignant transformation of B cells [16].

Finally, it is important to highlight the role of adipose tissue as an endocrine and paracrine organ that modulates the tumor microenvironment. In obesity, the overproduction of cytokines, adipokines, growth factors, and increased tissue hypoxia alters the communication between malignant cells and the stroma [17]. This favors disease progression and may impact the response to specific therapies, generating an additional challenge in the clinical management of B-cell lymphoma.

Clinical Implications

From a risk perspective, various meta-analyses (for example, those conducted by Castillo *et al*. in 2013 and Vera-Ponce *et al*. in 2024) [7,8] have demonstrated a significant association between obesity and lymphoma incidence, particularly in DLBCL. These studies indicate a dose-response relationship: as the body

mass index (BMI) increases, so does the risk of developing the disease. Such findings underscore the importance of considering obesity as a modifiable risk factor in primary prevention of B-cell lymphoma.

Regarding prognosis [9,11,13], they report that being overweight could be linked to better overall survival in patients with DLBCL, an observation that some authors call the "obesity paradox." The most accepted explanation suggests that adequate nutritional reserves could protect against treatment toxicity and allow better tolerance to chemotherapy. However, other studies indicate that excessively elevated BMI is associated with metabolic complications and comorbidities that worsen clinical evolution [18]

On the other hand, it has been observed that low weight and sarcopenia (loss of muscle mass) can negatively influence therapeutic response and survival. Research on body composition, such as that by Aleixo *et al*. (2022) [13], reveals that low visceral and subcutaneous adiposity is related to more unfavorable clinical outcomes. These findings reinforce the idea that beyond BMI, the distribution and quality of adipose and muscle tissue are key determinants in the evolution of patients with lymphoma.

In summary, the biological mechanisms linking obesity with B-cell lymphoma—chronic inflammation, alterations in adipokines, insulin resistance, and changes in the tumor microenvironment—directly affect the risk of developing the disease and its evolution. From a clinical perspective, identifying each patient's adiposity profile and nutritional status could guide personalized strategies for prevention, treatment, and support, thus contributing to a more comprehensive and effective management of B-cell lymphoma.

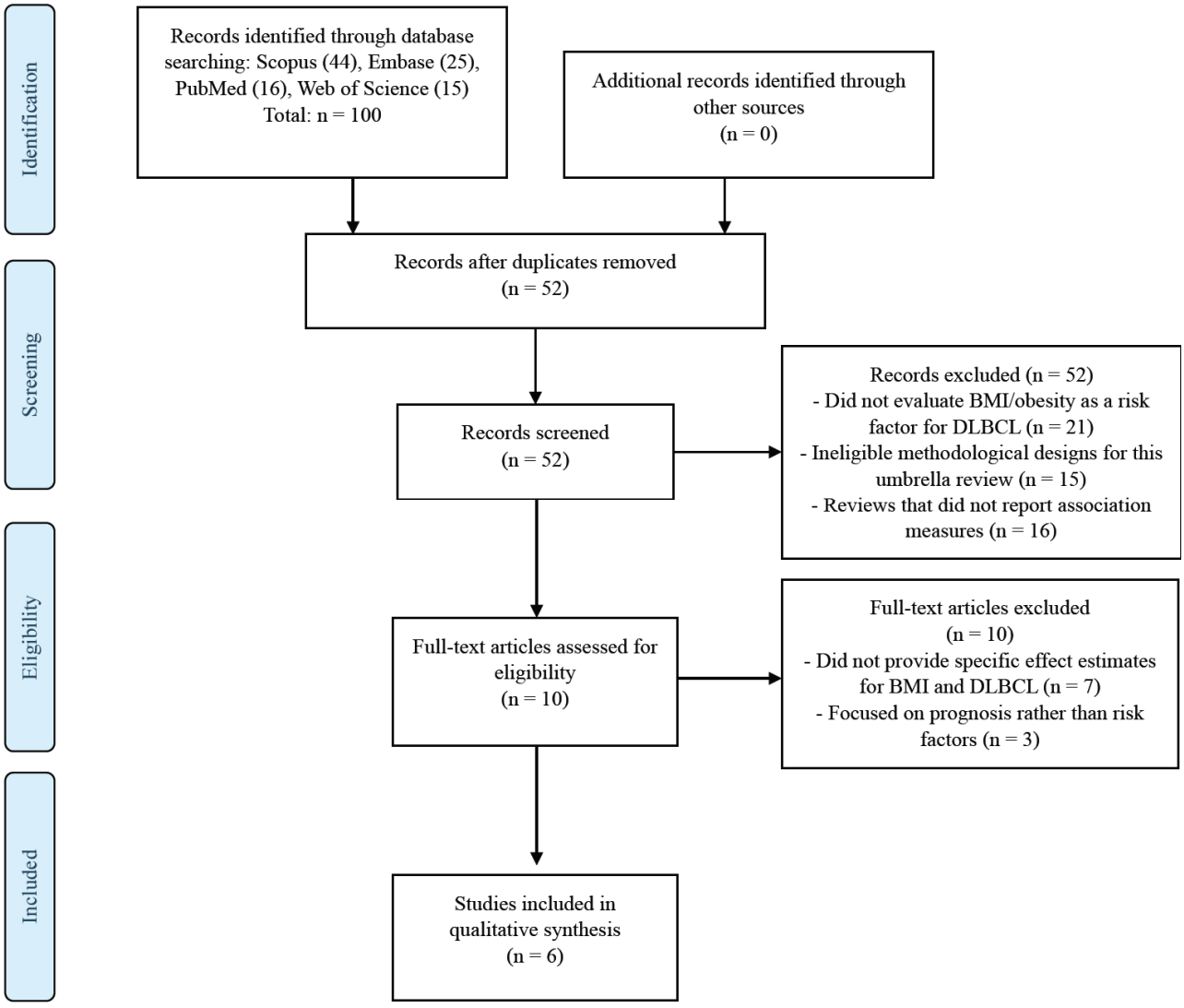

Figure 1: Flowchart of Study Selection.

Strengths and Limitations

A key strength of this umbrella review lies in the breadth of integrated evidence, as it gathers and compares findings from multiple meta-analyses and reviews on the relationship between obesity (measured through BMI and imaging methods) and B-cell lymphoma. This improves the statistical power and robustness of conclusions and allows the identification of consistent patterns (such as the dose-response relationship in DLBCL risk). Furthermore, the inclusion of studies evaluating the impact of obesity on both disease incidence and prognosis provides a more complete view, offering information on how the distribution and amount of adipose tissue can influence different phases of tumor progression. The systematic and global approach, with diverse populations, reinforces the external validity of the results and underscores the importance of body composition beyond BMI.

Among the limitations, the included studies' predominantly observational nature stands out, making it difficult to establish causal relationships and leaving open the possibility of confounding factors (such as lifestyles, comorbidities, or genetic variations). Likewise, heterogeneity in the definition of obesity and body composition can complicate the direct comparison of results. At the same time, publication bias may favor disseminating studies with statistically significant results. Finally, the dependence on secondary data and the lack of disaggregation by specific subgroups (for example, according to age, gender, or presence of comorbidities) may limit the clinical applicability of the findings, indicating the need for prospective studies with homogeneous measurement methods and greater detail in patient characterization.

CONCLUSIONS AND RECOMMENDATIONS

Collectively, the findings of this umbrella review reinforce the evidence of a significant association between obesity and B-cell lymphoma, mainly regarding the increased risk of developing DLBCL and the role that adiposity plays in patient prognosis. The proposed biological mechanisms—involving chronic inflammation, metabolic dysfunction, and hormonal alterations—explain a good part of this relationship; however, results on the effect of overweight and obesity on survival continue to be occasionally contradictory, highlighting the importance of considering factors such as adipose tissue distribution, overall nutritional status, and the presence of comorbidities. This panorama underscores the need to deepen research and adopt a comprehensive approach to the clinical management of these patients.

Given the potential impact of obesity on both the incidence and evolution of B-cell lymphoma, it is recommended to incorporate a detailed body composition assessment into clinical practice, ideally through imaging methods that allow distinguishing between fat and lean mass. Likewise, the development of nutritional and physical exercise interventions adapted to the particularities of each patient is pertinent, seeking to optimize their metabolic state and ability to tolerate intensive oncological treatments. Finally, it is advisable to undertake new longitudinal studies and clinical trials that include more diverse populations, employ standardized adiposity measurements, and analyze specific subgroups in greater detail to design more effective and personalized prevention and treatment strategies.

ACKNOWLEDGEMENTS

A special thanks to the members of Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Amazonas, Peru, for their support and contributions throughout the completion of this research.

FINANCIAL DISCLOSURE

This study was financed by Vicerectorado de Investigación de la Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

INFORMED CONSENT

This study is a review; therefore, informed consent is not required.

DATA AVAILABILITY

Data are available upon request to the corresponding author.

AUTHORS' CONTRIBUTION

Víctor Juan Vera-Ponce: Conceptualization, Investigation, Methodology, Resources, Writing - Original Draft, Writing - Review & Editing.

Fiorella E. Zuzunaga-Montoya: Methodology, Software, Data Curation, Formal analysis, Writing - Review & Editing.

Nataly Mayely Sanchez-Tamay: Validation, Investigation, Project administration, Writing - Original Draft, Writing - Review & Editing.

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Christian Humberto Huaman-Vega: Validation, Investigation, Methodology, Writing - Original Draft, Writing - Review & Editino.

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SUPPLEMENTARY FILE

The supplementary file can be downloaded from the journal website along with the article.

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Received on 15-02-2025 Accepted on 11-03-2025 Published on 22-04-2025

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