

RESEARCH ARTICLE

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Prevalence of Cancer Cachexia Among Breast Cancer Patients in Pakistan, Assessed Using the Mini-CASCO Scoring System

Rida Maria*, Fauzia Abdus Samad, Ammara Khalid, Shazaf Masood Sidhu

Abstract

Objective: This study aimed to estimate the prevalence, severity, and multidomain impact of cancer cachexia among Pakistani breast cancer patients, using the validated Mini-CASCO scoring system. **Methods:** We conducted an observational, cross-sectional study from February to December 2024 at Fauji Foundation Hospital (FFH), Rawalpindi. Eligible participants were female patients aged 18 years or older, with stage I–III breast cancer, receiving chemotherapy. Cachexia was assessed using the Mini-CASCO, which encompasses body composition, inflammation, anorexia, physical performance, and quality of life. Demographic, anthropometric, biochemical, and validated patient-reported outcomes were collected. Group differences between cachectic and non-cachectic patients were analyzed using the chi-square (χ^2) test, with statistical significance set at $p < 0.05$. **Results:** Of 134 participants (mean age: 45.2 ± 8.3 years), the prevalence of cachexia was 61.9% (95% CI: 53.4–70.0). The mean Mini-CASCO score was 45.7 ± 9.3 (95% CI: 43.7–47.8), indicating moderate cachexia. The severity distribution was 16.9% mild, 49.4% moderate, and 33.7% severe; no terminal cases were detected. Body weight and composition (12.7 ± 4.3) and anorexia (9.2 ± 2.6) were the most impaired domains. Compared with non-cachectic patients, those with cachexia had significantly greater inflammation (11.2 vs. 7.4, $p < 0.001$), anorexia (10.9 vs. 6.8, $p < 0.001$), and poorer quality of life (6.2 vs. 4.7, $p < 0.001$). **Conclusion:** More than six in ten patients exhibited cachexia a rate substantially higher than global estimates highlighting its neglected burden in low- and middle-income country (LMIC) oncology settings. Early, structured assessment using the Mini-CASCO, along with the integration of multimodal nutritional and supportive interventions, is urgently needed to reduce preventable morbidity and mortality. Future multicenter, longitudinal studies are essential to guide evidence-based cachexia management in LMICs.

Keywords: Breast cancer- cachexia- Mini-CASCO- body composition- inflammation- LMICs- South Asia

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Introduction

Cancer remains a leading cause of morbidity and mortality worldwide, with breast cancer representing the most common malignancy among women, particularly in LMICs such as Pakistan [1]. According to Global Cancer Observatory (GLOBOCAN 2020), breast cancer accounts for nearly one-third of all female cancers in Pakistan, with incidence and mortality rates among the highest in South Asia [2]. Beyond the malignancy itself, a substantial proportion of patients experience cancer cachexia, a complex metabolic syndrome characterized by severe weight loss and muscle wasting that contributes to poor treatment outcomes and accounts for an estimated 20–30% of cancer-related deaths globally [3, 4].

Cancer cachexia is defined as progressive skeletal muscle loss, with or without adipose tissue loss that cannot be fully reversed by conventional nutritional support [5]. Its presence impairs treatment tolerance, increases chemotherapy toxicity, and shortens survival. The syndrome arises from multifactorial mechanisms,

including reduced dietary intake, systemic inflammation, and profound metabolic alterations [6]. In LMICs such as Pakistan where delayed diagnosis, limited supportive care, and constrained health system resources already hinder cancer management, the impact of cachexia is likely underrecognized yet deeply detrimental to survival and quality of life.

Despite its clinical significance, early identification of cachexia remains challenging due to heterogeneous definitions and delayed clinical recognition. Historically, unintentional weight loss ($\geq 5\%$ over 6 months) served as the principal diagnostic threshold [6]. More recently, diagnostic frameworks have evolved toward multidimensional approaches that integrate body composition, systemic inflammation, physical performance, and quality of life [7]. Validated instruments such as the Cancer Cachexia Score (CASCO) and its abbreviated version, the Mini-CASCO, now enable structured staging and multi-domain assessment, offering a more comprehensive understanding of cachexia in routine oncology practice [8, 9].

Department of Medical Oncology, Fauji Foundation Hospital Rawalpindi, Pakistan. *For Correspondence: ridamaria593@gmail.com

Global systematic reviews (2022–2024) estimate a cachexia prevalence of approximately 30–35% across cancers, but most evidence originates from high-income settings, creating major gaps relevant to LMICs [10]. In Pakistan, nutritional and functional assessments are rarely integrated into cancer care pathways, resulting in systematic under-diagnosis and missed opportunities for timely intervention [11]. No studies from South Asia, including Pakistan, have evaluated cachexia using the Mini-CASCO tool, despite its growing adoption in international research. As a result, the multidimensional clinical profile of cachexia in Pakistani patients remains unexplored. Addressing this gap is critical to aligning regional practice with international standards and enabling earlier identification of high-risk patients.

This study addresses this critical gap by investigating the prevalence and severity of cancer cachexia among breast cancer patients in Pakistan using the Mini-CASCO scoring system. By applying Mini-CASCO in a Pakistani cohort for the first time, this study advances current diagnostic practice by introducing structured, domain-based cachexia profiling that aligns with global evidence-based standards. The primary objective of this study is to determine the prevalence and severity of cancer cachexia among breast cancer patients using the Mini-CASCO instrument. Secondary objectives include comparing Mini-CASCO domain scores between cachectic and non-cachectic patients and identifying patterns of impairment across multidimensional domains. These objectives provide a clear rationale and logical bridge between the introduction and subsequent methodological approach. By generating locally relevant evidence, this study aims to inform the integration of structured cachexia screening and management into oncology care in Pakistan and to explore opportunities for implementing nutritional interventions.

Materials and Methods

This observational cross-sectional study was conducted between February and December 2024 at the Department of Medical Oncology, Fauji Foundation Hospital (FFH) Rawalpindi, Pakistan. FFH is a major tertiary-care teaching hospital and is recognized for its comprehensive oncology services. The hospital offers multidisciplinary supportive care, including dietitian-led nutritional assessment and counseling, individualized nutrition plans for chemotherapy patients, and access to supplementary nutritional products when clinically indicated. Ethical approval was obtained from the Institutional Review Board (Approval No. 794/RC/FFH/RWP). Written informed consent was obtained, with thumb impressions verified for illiterate participants.

Eligible participants included females aged ≥ 18 years with histologically confirmed stage I–III breast cancer who had received at least one cycle of chemotherapy. Cachexia scoring was performed prior to radiotherapy or surgery, and all assessments were conducted soon after completion of neoadjuvant chemotherapy (NAC) to capture the early post-treatment nutritional and inflammatory status of patients. Patients with metastatic disease, non-cancer-related malnutrition, gastrointestinal

or endocrine disorders, pregnancy, pre-existing nutritional syndromes, severe mobility limitation, or concurrent malignancies were excluded.

Sample size was calculated using the single population proportion formula:

$$n = \frac{Z^2 \times p \times (1 - p)}{d^2}$$

Where $n = Z^2 \times p \times (1 - p) / d^2$, where $Z = 1.96$ (95% confidence), $p = 0.5$ (assumed prevalence of cachexia), and $d = 0.083$ (precision). A precision level of 0.083 was selected to ensure an adequately powered yet feasible sample size, as no prior local prevalence data were available and a smaller precision (e.g., 0.05) would have required an unrealistically large sample for a single-center study.

$$n = \frac{(1.96)^2 \times 0.5 \times (1 - 0.5)}{(0.083)^2} = 140$$

The required sample size was 126; after accounting for 10% attrition, a total of 140 patients were targeted. This ensured 80% power at $\alpha = 0.05$. The final effective sample size after exclusions was 134 patients, with subgroup analyses performed on 83 cachectic and 51 non-cachectic patients. This study used a single-center convenience sampling approach, which may limit external validity and generalizability.

Data collection included demographic, anthropometric, biochemical, and patient-reported measures. Weight history for the preceding six months was obtained from medical records and confirmed by patient recall. Body composition was assessed using calibrated bioelectrical impedance analysis (BIA) under standardized conditions. BIA was selected due to its feasibility, affordability, and accessibility in low- and middle-income country (LMIC) clinical settings, despite known limitations in accuracy compared with dual-energy X-ray absorptiometry (DXA). Biochemical parameters such as C-reactive protein (CRP), albumin, hemoglobin, and absolute lymphocyte count (ALC) were retrieved from hospital records. Appetite, performance status, and quality of life were evaluated using validated tools, including the Simplified Nutrition Appetite Questionnaire (SNAQ) with language validation for the local population, Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30) adapted and validated for Urdu-speaking participants.

Cachexia was defined according to international consensus criteria as weight loss $> 5\%$ in the previous six months, or body mass index (BMI) $< 20 \text{ kg/m}^2$ with $> 2\%$ weight loss, or sarcopenia with $> 2\%$ loss. Cachexia diagnosis using the Mini-CASCO (Cancer Cachexia Score) scoring system was operationalized as follows: body weight and composition (BWC, 0–40), inflammatory/metabolic/immune disturbances (IMD, 0–20), physical performance (PHP, 0–15), anorexia (ANO,

0–15), and quality of life (QOL, 0–10); total score = sum of domain scores. Missing variables prior to imputation were handled using multiple imputations under missing-at-random assumptions. Cutoff thresholds were defined as mild (0–25), moderate (26–50), severe (51–75), and terminal (76–100).

Data quality was ensured using inter-observer reliability assessments with two independent raters and agreement was measured using intraclass correlation coefficients (ICC) for continuous variables and Cohen's kappa for categorical items. ICC values ranged from 0.82–0.91, indicating excellent reliability, and double-entry verification. Overall, 7.4% of biochemical and anthropometric variables were missing and subsequently imputed to preserve statistical power.

All analyses were performed using SPSS version 21 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize participant demographics, anthropometric measures, biochemical indices, and Mini-CASCO scores. Continuous variables were expressed as mean \pm standard deviation (SD) with 95% confidence intervals (CI), and categorical variables were expressed as frequencies and percentages. Normality of continuous variables was assessed using the Shapiro–Wilk test. For normally distributed variables, independent-samples t-tests were used to compare means between cachectic and non-cachectic patients. For non-normally distributed variables, the Mann–Whitney U test was applied.

Categorical variables were compared using χ^2 or Fisher's exact tests as appropriate, with statistical significance set at $p < 0.05$.

Results

Of the 140 eligible patients, 134 were included in the final analysis, yielding a response rate of 95.7%. The mean age was 45.2 ± 8.3 years, with most participants between 41–50 years (39.6%). Weight loss over the preceding six months was substantial: 32.9% reported $\leq 10\%$ loss, while 67.1% reported $>10\%$ loss, including 24.6% with severe (16–20%) and 22.4% with very severe ($> 20\%$) loss. Loss of lean body mass assessed by BIA was present in 71.6% of participants.

Biochemical indices indicated pronounced systemic inflammation and malnutrition, with elevated CRP (> 10 mg/L) in 76.1%, hypoalbuminemia (< 3.2 g/dL) in 65.7%, and lymphopenia ($< 1500/\text{mm}^3$) in 74.6%. Cachexia prevalence and severity were also presented, showing that 61.9% of patients met criteria for cachexia, with 16.9% mild, 49.4% moderate, and 33.7% severe; no patients had terminal cachexia (Table 1).

Based on Mini-CASCO assessments, the mean total score was 45.7 ± 9.3 , corresponding to moderate cachexia. Domain-specific scores showed the highest impairment in body weight/composition (BWC) and anorexia (ANO), while physical performance (PHP) and quality of life

Table 1. Baseline Clinical, Anthropometric, and Inflammatory Characteristics of Female with Breast Cancer (N = 134)

Variable	Category	Frequency (n)	Percentage (%)
Age group (years)	20–30	9	6.7
	31–40	39	29.1
	41–50	53	39.6
	51–60	33	24.6
Mean age: 45.2 ± 8.3 years (95% CI: 43.8–46.6)			
Weight loss (6-month)	Mild ($\leq 5\%$)	21	15.7
	Moderate (6–10%)	23	17.2
	High (11–15%)	27	20.1
	Severe (16–20%)	33	24.6
	Very severe ($> 20\%$)	30	22.4
Lean body mass (BIA)	Unchanged	38	28.4
	Loss	96	71.6
CRP (mg/L)	≤ 10	32	23.9
	> 10 to ≤ 20	50	37.3
	> 20	52	38.8
Albumin (g/dL)	≥ 3.2	46	34.3
	< 3.2	88	65.7
Absolute lymphocyte count ($/\text{mm}^3$)	≥ 1500	34	25.4
	< 1500	100	74.6
Cachexia status	Non-cachectic	51	38.1
	Cachectic (total)	83	61.9
Cachexia severity (among cachectic patients, n = 83)	Mild	14	16.9
	Moderate	41	49.4
	Severity	28	33.7
	Terminal	0	0.0

Table 2. Mini-CASCO Domain Scores and Total Cachexia Burden

Domain	Maximum score	Mean \pm SD	Median (IQR)	Range
BWC (Weight loss, Lean body mass)	40	12.7 \pm 4.3	13 (10–15)	6–22
IMD (CRP, Albumin, TLC)	20	9.6 \pm 2.5	10 (8–11)	5–17
PHP (Physical performance)	15	8.4 \pm 2.3	8 (7–10)	5–14
ANO (SNAQ)	15	9.2 \pm 2.6	9 (8–11)	6–15
QOL (EORTC QLQ-C30)	10	5.6 \pm 1.1	6 (5–7)	3–8
Total Mini-CASCO	100	45.7 \pm 9.3	46 (40–52)	28–70

Table 3. Comparison of Age and Mini-CASCO Domains between Cachexia and Non-Cachexia Patients

Variable	Cachectic (n=83) Mean \pm SD	Non-cachectic (n=51) Mean \pm SD	Mean difference	95% CI	Cohen's d	p-value
Age (years)	46.1 \pm 8.5	43.7 \pm 7.9	2.4	–0.4 to 5.2	0.29	0.09
BWC	14.9 \pm 4.0	8.1 \pm 2.8	6.8	5.6–8.0	1.97	< 0.001
IMD	11.2 \pm 2.7	6.4 \pm 2.1	4.8	3.9–5.7	1.99	< 0.001
PHP	9.8 \pm 2.4	5.5 \pm 1.9	4.3	3.5–5.1	2	< 0.001
ANO	10.9 \pm 2.6	5.8 \pm 1.8	5.1	4.2–6.0	2.23	< 0.001
QOL	6.2 \pm 1.2	3.7 \pm 1.0	2.5	2.1–2.9	2.26	< 0.001
Total Mini-CASCO	52.1 \pm 7.8	33.5 \pm 6.9	18.6	15.9–21.3	2.49	< 0.001

(QOL) were moderately affected (Table 2).

Comparative analysis between cachectic (n = 83) and non-cachectic (n = 51) groups showed statistically significant differences across all Mini-CASCO domains. Cachectic patients had greater impairment in body composition (14.9 \pm 4.0 vs. 8.1 \pm 2.8), systemic inflammation (11.2 \pm 2.7 vs. 6.4 \pm 2.1), physical performance (9.8 \pm 2.4 vs. 5.5 \pm 1.9), anorexia (10.9 \pm 2.6 vs. 5.8 \pm 1.8), and quality of life (6.2 \pm 1.2 vs. 3.7 \pm 1.0), all with $p < 0.001$. Effect sizes confirmed both the magnitude and clinical relevance of these differences. The mean difference in total Mini-CASCO score was 18.6 points (95% CI 15.9–21.3; Cohen's d = 2.49), indicating a very large effect. Domain-specific mean differences also demonstrated large effect sizes: BWC (6.8 points; 95% CI 5.6–8.0; d = 1.97), IMD (4.8 points; 95% CI 4.1–5.5; d = 1.91), PHP (4.3 points; 95% CI 3.6–4.9; d = 1.86), ANO (5.1 points; 95% CI 4.4–5.9; d = 1.98), and QOL (2.5 points; 95% CI 2.1–2.9; d = 2.26) (Table 3).

Discussion

Cancer cachexia, a multifactorial syndrome marked by involuntary weight loss, systemic inflammation, metabolic derangements, and functional decline, was systematically evaluated in this study using the validated Mini-CASCO scoring system [12]. Our prevalence of 61.9% among female breast cancer patients represents the first report from Pakistan employing Mini-CASCO and indicates a substantial, underrecognized burden. The prevalence of cachexia observed in this study was almost double the global pooled estimate of 33% among cancer patients across all stages. This global figure is derived from a recent systematic review and meta-analysis encompassing more than 125 studies and nearly 138,000 patients [13].

In comparison, European cohorts applying

CASCO-based approaches report prevalence rates of only 27–30%, while studies from HICs such as the United States similarly document around 30% [14]. Comparable data from LMICs show variability, for example, an Indonesian breast cancer cohort reported prevalence of 38.1% using Fearon's criteria and only 20.0% according to Evans' definition [15]. Broader Asian evidence indicates highly heterogeneous prevalence ranging from 6.2% to 93%, reflecting differences in diagnostic criteria, tumor sites, and healthcare resources [16].

Our higher prevalence highlights a disproportionate burden in LMICs, plausibly due to late presentation, lower baseline nutritional reserves, and lack of structured nutritional support. Importantly, the mechanistic interplay between inflammation, anorexia, and accelerated lean mass depletion provides a biologically plausible explanation for the high burden observed in this cohort. Persistent systemic inflammation evidenced by significant elevated CRP and hypoalbuminemia in our study likely drives anorexia through cytokine-mediated appetite suppression, which in turn exacerbates negative energy balance. This inflammatory–anorexia–catabolism axis accelerates muscle proteolysis and impairs anabolic recovery, thereby amplifying the severity of cachexia in settings where dietary intake is already compromised. Such interconnected pathways highlight the need for biologically informed, multimodal interventions rather than isolated nutritional strategies.

In terms of severity, most patients presented with moderate (49.4%) or severe (33.7%) cachexia, while only 16.9% fell in the mild category and none had terminal cachexia. This contrasts sharply with European reports where up to 40–45% of cachectic patients are classified as mild, reflecting earlier diagnosis and more proactive interventions [17]. Conversely, our distribution aligns with Indonesian data where 50–57% of patients fell

into moderate-to-severe categories [16]. This pattern reinforces the LMIC-specific reality such as delayed presentation, limited dietetic input, and constrained rehabilitation contribute to more advanced cachexia at diagnosis. The absence of terminal cachexia likely reflects outpatient sampling bias rather than true epidemiology.

Domain-level analysis revealed the greatest impairment in body weight/composition and anorexia, consistent with LMIC literature where caloric insufficiency and systemic inflammation drive rapid lean mass depletion [18-20]. In contrast, physical performance and quality of life were moderately compromised; suggesting functional decline may lag behind nutritional deterioration, creating a potential therapeutic window for early intervention. However, it remains unclear whether impairments observed in appetite, inflammation, or physical function preceded the onset of cachexia or emerged as consequences of the cachexia state. This temporal uncertainty is particularly relevant given ongoing chemotherapy, as treatment-related toxicities could independently induce anorexia, fatigue, or inflammation. Integrating this limitation into interpretation is essential, as it restricts the ability to disentangle causality between domain impairments and cachexia severity.

Evidence from HICs shows greater preservation of function and QoL due to structured rehabilitation, appetite management, and earlier detection [21-23]. Our results emphasize the need for routine screening of appetite and composition, not just weight loss, to identify patients at high risk before irreversible decline. Comparison with regional malnutrition studies reinforces this context as prior Pakistani data show high rates of under-nutrition and micronutrient deficiencies among women with cancer even before treatment initiation, which may compound susceptibility to cachexia despite differing measurement tools.

Comparative analysis confirmed significantly greater impairment across Mini-CASCO domains among cachectic patients versus non-cachectic peers, reinforcing that cachexia imposes a multidimensional burden encompassing physiological, inflammatory, and psychosocial processes. These findings highlight opportunities for earlier detection, including routine appetite screening, inflammatory marker tracking, and targeted assessment of body composition before functional decline becomes irreversible. To strengthen the clinical and policy relevance, practical pathways for integrating Mini-CASCO into oncology and palliative care should be emphasized. Mini-CASCO could be incorporated at baseline staging visits, repeated before each chemotherapy cycle, and linked to structured referral pathways involving dietitians, physiotherapists, and psycho-oncology services. Embedding Mini-CASCO scoring into electronic medical records would allow automated alerts for high-risk patients and facilitate multidisciplinary case discussions. Such pragmatic integration aligns with global calls for standardized cachexia assessment within cancer care.

Our findings demand system-level recognition of cachexia as a critical, yet neglected, determinant of survival and quality of life. While the “system-level

recognition” theme remains important, streamlining this content emphasizes the need for actionable steps rather than extensive policy narrative. Routine cachexia screening, low-cost nutritional interventions, affordable protein supplementation, and simplified rehabilitation strategies should be prioritized in LMIC oncology settings. Explicitly linking these findings to prevention strategies such as pre-habilitation, dietary optimization before chemotherapy and monitoring of early inflammatory shifts aligns with global evidence that early intervention can blunt cachexia progression.

Limitations

The cross-sectional design precludes causal or temporal inference, and the single-center nature limits generalizability across Pakistan. Use of bioelectrical impedance rather than gold-standard imaging (CT or DXA) may have reduced lean body mass precision, though pragmatic feasibility justified this choice in our LMIC context. Nevertheless, applying a standardized multidimensional tool is a major strength, offering the first comprehensive cachexia dataset in Pakistan. Future research should prioritize longitudinal, multicenter studies to establish temporal trajectories of cachexia progression and evaluate intervention efficacy.

In conclusion, this study reveals a significantly high burden of cancer cachexia among Pakistani breast cancer patients, with more than 60% experiencing moderate to severe disease substantially higher than global estimates. The multidimensional impairment demonstrated through Mini-CASCO profiling highlights the urgent need for structured cachexia screening in routine oncology care. Our findings highlight that systemic inflammation, anorexia, and muscle loss remain key predictors of disease severity, and their early detection could significantly improve treatment compliance and clinical outcomes. Integrating Mini-CASCO into oncology pathways, coupled with feasible LMIC-appropriate interventions including nutrition counseling, inflammation-directed strategies, and physical rehabilitation may help mitigate this burden.

Given the cross-sectional nature of the study and reliance on self-reported weight history, longitudinal multicenter research is critically needed to validate these findings and inform national cachexia management strategies in Pakistan and other LMICs.

Author Contribution Statement

RM and FAS: study conception and design, methodology development, data analysis, interpretation, manuscript drafting, and overall supervision. AK and SMS: data collection, data curation, and manuscript review. All authors approved the final version of the manuscript and agree to be accountable for the accuracy and integrity of the work.

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Role of the Funder

No funding bodies had any role in study design, data collection, data analysis, interpretation, or manuscript preparation.

Ethical Approval

The study was conducted in accordance with institutional and national ethical guidelines. Ethical approval was granted by the Institutional Review Board of Fauji Foundation Hospital, Rawalpindi (Approval No. 794/RC/FFH/RWP). Written informed consent was obtained from all participants; thumb impressions were obtained from illiterate participants.

Protocol and Registration

This study was not registered in any clinical trial registry because it was a non-interventional, observational, cross-sectional design for which registration is not mandated.

Data Availability

The dataset generated and analyzed in this study is available from the corresponding author upon reasonable request.

Consent for Publication

Not applicable; no identifiable personal data are included.

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