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# THE HIDDEN BURDEN: A PSYCHODERMATOLOGICAL ANALYSIS OF CHRONIC PRURITUS IN CANCER PATIENTS AND THE AMPLIFYING EFFECT OF SYSTEMIC COMORBIDITIES

Dermatology

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## ABSTRACT

**Background:** Chronic pruritus (CP) is a distressing yet frequently under-recognized symptom in cancer patients, contributing substantially to psychological distress, sleep disturbance, and functional impairment[1,2]. Although malignancy-related systemic inflammation initiates pruritus, the extent to which coexisting medical and surgical comorbidities amplify itch severity and quality-of-life (QoL) deterioration remains insufficiently explored[3]. **Objective:** To evaluate the psychosocial burden of chronic pruritus in cancer patients and to identify systemic comorbidities that act as key amplifiers of itch severity and QoL impairment. **Methods:** A cross-sectional observational study was conducted among 85 cancer patients experiencing chronic pruritus for more than six weeks. Pruritus severity was assessed using the **Numerical Rating Scale (NRS)**[4], and QoL impairment was measured using the **Dermatology Life Quality Index (DLQI)**[3]. Patients were stratified based on associated medical and surgical comorbidities. Statistical analysis included analysis of variance and Pearson's correlation coefficient. **Results:** Hypothyroidism was associated with the highest itch severity (mean NRS

## KEYWORDS

Chronic Pruritus; Onco-dermatology; Quality of Life; DLQI; Comorbidity; Cancer

## INTRODUCTION

Cancer is a life-altering diagnosis that profoundly affects physical health, emotional well-being, and social functioning. Beyond pain, fatigue, and weight loss, chronic pruritus (CP) has emerged as one of the most distressing yet under-recognized symptoms in oncology patients[1,2]. Persistent itch interferes with sleep, concentration, mood, interpersonal relationships, and overall quality of life (QoL), often to a degree disproportionate to its apparent clinical severity[3].

Chronic pruritus, defined as itch persisting for more than six weeks, is a complex condition resulting from dysregulated interactions between the skin, immune system, and nervous system[1]. In cancer patients, pruritus may arise from multiple mechanisms, including paraneoplastic processes, tumor-derived cytokine release, chemotherapy- or immunotherapy-induced immune activation, metabolic derangements, and organ dysfunction[2]. Importantly, malignancy itself induces a state of chronic systemic inflammation that lowers neural itch thresholds, rendering patients particularly vulnerable to pruritogenic stimuli[5].

Emerging evidence suggests that coexisting systemic comorbidities further modify the pruritic experience in oncology patients. Medical conditions such as diabetes mellitus, hypothyroidism, asthma, dyslipidemia, and cardiovascular disease can influence itch perception by altering epidermal barrier integrity, peripheral nerve sensitivity, and immune signaling pathways[1,5]. Similarly, prior surgical interventions-especially endocrine and hepatobiliary procedures-may exert long-term effects on neuro-immune homeostasis, thereby modulating pruriceptive signaling[6].

Despite increasing recognition of chronic pruritus as a major contributor to patient suffering, oncological care pathways largely prioritize tumor control, often overlooking patient-reported outcomes such as itch severity and QoL impairment. Contemporary guidelines on chronic pruritus emphasize the importance of identifying systemic contributors and assessing psychosocial impact; however, data specifically examining the combined influence of medical and surgical comorbidities on pruritus burden in cancer patients remain limited, particularly from developing regions[3].

Against this background, the present study aims to evaluate the burden of chronic pruritus in cancer patients through a psychodermatological and Onco-Dermatology lens, with particular emphasis on quality-of-life impairment. By examining the influence of associated medical and surgical comorbidities on itch severity and QoL, this study seeks to identify high-risk phenotypes and support a more integrated, patient-centered approach to pruritus management in oncology.

## MATERIALS AND METHODS

### Study Design and Setting

A hospital-based cross-sectional observational study was conducted between March 2021 and June 2022 at the Department of Dermatology, Venereology and Leprology, in collaboration with the Department of Oncology, Geetanjali Medical College and Hospital (GMCH), Udaipur, Rajasthan, India.

### Study Population

A total of 85 consecutive cancer patients (n = 85) presenting with chronic pruritus were enrolled during the study period after obtaining written informed consent.

### Inclusion Criteria

- Age ≥18 years
- Histopathologically or clinically confirmed diagnosis of malignancy
- Presence of chronic pruritus lasting ≥6 weeks, in accordance with international definitions[1,3]
- Ability to understand and respond in Hindi or English

### Exclusion Criteria

- Use of topical or systemic antipruritic therapy within the preceding three weeks
- Cognitive impairment or severe systemic illness precluding reliable questionnaire completion

### Data Collection

Data were collected using a structured proforma and included:

- Sociodemographic details (age, sex)
- Type and duration of malignancy
- Medical comorbidities, including diabetes mellitus, hypertension, hypothyroidism, asthma, and dyslipidemia
- Surgical comorbidities, including thyroidectomy, cholecystectomy, hernia repair, varicose vein surgery, and appendectomy

### Assessment of Pruritus Severity

Pruritus severity was assessed using the Numerical Rating Scale

(NRS), a validated patient-reported outcome measure for chronic itch[4]. Patients rated their average itch intensity over the preceding week on a scale ranging from 0 (no itch) to 10 (worst imaginable itch).

### Assessment of Quality of Life

Quality-of-life impairment was evaluated using the Dermatology Life Quality Index (DLQI), a widely validated instrument recommended in chronic pruritus assessment[3]. The DLQI consists of 10 questions assessing the impact of skin symptoms on daily activities, sleep, work, social interactions, and emotional well-being. Total scores range from 0 to 30, with higher scores indicating greater impairment.

### Statistical Analysis

Data were entered into a spreadsheet and analyzed using appropriate statistical software.

- Continuous variables were expressed as mean ± standard deviation (SD)
- Categorical variables were expressed as frequency and percentage
- Mean NRS and DLQI scores across medical and surgical comorbidity groups were compared using analysis of variance (ANOVA)
- The relationship between itch severity and quality-of-life impairment was assessed using Pearson's correlation coefficient
- A p-value < 0.05 was considered statistically significant

### Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Geetanjali Medical College and Hospital, Udaipur. Written informed consent was obtained from all participants prior to enrollment.

## RESULTS

### Demographic Characteristics of the Study Population

A total of 85 cancer patients (n = 85) with chronic pruritus were included in the study. The mean age of the participants was 49.9 ± 13.7 years, with the majority of patients aged ≥50 years. The male-to-female ratio was 0.9:1, indicating a near-equal gender distribution.

Statistical analysis revealed no significant association between age or sex and pruritus severity (NRS) or quality-of-life impairment (DLQI) ($p > 0.05$). This indicates that demographic variables did not significantly influence the pruritic burden in the study population.

### Medical Comorbidities and Pruritic Burden

Medical comorbidities were commonly observed among the study participants. Diabetes mellitus was the most prevalent comorbidity (30.5%), followed by hypertension (27%) and hyperlipidemia (12.9%). Despite their higher prevalence, these metabolic comorbidities were associated with only moderate itch severity and QoL impairment, suggesting a relatively limited impact on pruritic burden.

In contrast, endocrine and respiratory comorbidities demonstrated a disproportionately higher impact. Patients with hypothyroidism reported the highest mean itch severity (NRS 6.20 w1.69)while those with asthma exhibited the greatest quality-of-life impairment (DLQI 14.50w5.29).

Patients without any documented medical comorbidity also showed notable DLQI scores, indicating that malignancy-related factors alone may contribute significantly to QoL impairment in chronic pruritus[1,2].

**Table 1: Medical Comorbidities and Their Impact on Pruritus (n=85)**

| Medical Condition | Prevalence n (%) | Mean NRS (Itch Severity) | Mean DLQI (QoL Impairment) | Potential Mechanism |
|---|---|---|---|---|
| Hypothyroidism | 10 (11.7%) | 6.20 ± 1.69 | 10.90 ± 6.26 | Barrier dysfunction & Xerosis |
| Asthma | 8 (9.4%) | 6.13 ± 1.64 | 14.50 ± 5.29 | Th2-mediated neuroinflammation |
| Hyperlipidemia | 11 (12.9%) | 5.55 ± 2.38 | 14.45 ± 8.24 | Systemic inflammatory markers |
| Hypertension | 23 (27.0%) | 5.26 ± 2.47 | 14.04 ± 7.62 | Medication-induced xerosis |
| Diabetes Mellitus | 26 (30.5%) | 4.73 ± 2.54 | 12.85 ± 7.09 | Microvascular/ Neuropathic itch |
| No Comorbidity | 7 (8.2%) | 5.29 ± 1.25 | 15.57 ± 2.37 | Malignancy-driven pathways |

### Surgical Comorbidities and Pruritic Burden

Among surgical comorbidities, hernia repair (23.5%) and varicose vein surgery (22.3%) were the most frequently reported procedures. Varicose vein surgery was associated with relatively higher itch severity (NRS 5.68w1.89)and moderate-to-severe DLQI scores, reflecting localized pruritus related to venous insufficiency[1].

The surgical data revealed a distinct pattern. While cholecystectomy showed a notable impact on pruritus burden, thyroidectomy demonstrated the most pronounced impairment in daily functioning, with a mean DLQI of 14.75w8.58

Interestingly, patients with no prior surgical history exhibited the highest overall DLQI scores, suggesting that advanced or non-operable malignancy may be associated with greater systemic inflammatory burden and psychosocial distress[2].

**Table 2: Surgical Comorbidities and their Impact on Pruritus (n=85)**

| Surgical History | Prevalence n (%) | Mean NRS (Itch Severity) | Mean DLQI (QoL Impairment) | Key Observation |
|---|---|---|---|---|
| Thyroid Surgery | 12 (14.1%) | 5.67 ± 2.61 | 14.75 ± 8.58 | Highest QoL disruption |
| Varicose Veins | 19 (22.3%) | 5.68 ± 1.89 | 13.84 ± 6.70 | Stasis-related localized itch |
| Cholecystectomy | 10 (11.7%) | 5.40 ± 2.17 | 14.30 ± 6.88 | Bile acid metabolism shift |
| Hernia Repair | 20 (23.5%) | 5.20 ± 2.35 | 13.35 ± 6.92 | Post-op inflammatory memory |
| Appendicectomy | 15 (17.6%) | 4.87 ± 2.53 | 9.93 ± 4.96 | Minimal systemic impact |
| No Surgery | 9 (10.5%) | 5.11 ± 2.37 | 16.78 ± 6.26 | Advanced/Inoperable status |

### Correlation Between Itch Severity and Quality of Life

Pearson's correlation analysis demonstrated a strong and statistically significant positive correlation between itch severity and quality-of-life impairment across the entire cohort (r=0.65, pl0.001). This finding indicates that increasing pruritus intensity was directly associated with worsening QoL, reinforcing itch severity as a major determinant of patient-reported disability[3,4].

**Table 3: Correlation Analysis (NRS vs. DLQI)**

| Statistical Parameter | Value | Interpretation |
|---|---|---|
| Pearson's Coefficient (r) | 0.65 | Strong Positive Correlation |
| P-Value | < 0.001 | Highly Statistically Significant |

### Regional and Environmental Context

As the study was conducted in Udaipur, Rajasthan, a region characterized by hot and arid climatic conditions, environmental xerosis may have contributed to baseline skin dryness. This factor may have further exacerbated pruritic symptoms, particularly in patients with endocrine comorbidities[1,2].

## DISCUSSION

The present study highlights that chronic pruritus (CP) in cancer patients is not merely a secondary dermatological complaint but a complex psychodermatological manifestation driven by sustained neuro-immune dysregulation. The strong positive correlation between itch severity and quality-of-life (QoL) impairment *($r = 0.65, p < 0.001$)* underscores that the subjective intensity of pruritus is a principal determinant of psychosocial disability in oncology patients. This finding is consistent with existing literature that identifies pruritus as one of the most distressing non-pain symptoms in systemic disease and malignancy[1–3].

Importantly, demographic variables such as age and sex did not significantly influence either itch severity or QoL impairment in the present cohort. This observation suggests that biological vulnerability and systemic disease interactions outweigh demographic determinants in shaping the pruritic burden among cancer patients. Such findings reinforce the need to focus on disease-specific and comorbidity-related factors when evaluating pruritus in oncology settings[2,3].

### The Double-Hit Hypothesis: Cancer-Primed Inflammation and Comorbidity-Driven Amplification

The findings of this study strongly support a "double-hit" hypothesis,

wherein malignancy provides the first hit by inducing chronic systemic inflammation, and coexisting medical or surgical comorbidities provide a second hit by disrupting skin barrier integrity or neural signaling pathways. Together, these insults amplify pruriceptive signaling and intensify patient suffering[1,2].

Hypothyroidism emerged as the medical comorbidity associated with the highest itch severity in this cohort. Thyroid hormone deficiency is known to impair epidermal lipid synthesis, reduce sebaceous and eccrine gland activity, and alter keratinocyte differentiation, leading to pronounced xerosis and barrier dysfunction[1,2]. In a cancer-primed inflammatory environment, this compromised barrier facilitates deeper penetration of pruritogenic mediators and heightened activation of peripheral C-nerve fibers, resulting in intensified itch perception. These mechanisms align with previous studies linking endocrine dysfunction to chronic pruritus in systemic disease[1].

Asthma was associated with the greatest QoL impairment despite comparable itch intensity to other comorbidities. This disproportionate psychosocial burden likely reflects shared Th2-mediated immune pathways. Cytokines such as interleukin-4 (IL-4) and interleukin-13 (IL-13), central to asthma pathogenesis, are also potent pruritogens capable of directly sensitizing sensory neurons5. When malignancy-related inflammation converges with an atopic systemic profile, the resulting pruritus is often persistent, treatment-resistant, and profoundly disruptive to daily functioning[2,5].

### Surgical Comorbidities and the Concept of Inflammatory Memory

The significant variation in QoL impairment across surgical comorbidity groups suggests that surgical interventions may exert long-term modulatory effects on neuro-immune balance. Thyroidectomy was associated with the most pronounced QoL impairment, possibly reflecting postoperative endocrine instability and altered neuro-immune signaling pathways[6]. Cholecystectomy also demonstrated a notable pruritic burden, which may be related to alterations in bile acid metabolism and systemic inflammatory responses known to influence itch pathways[2].

An intriguing finding was the severe QoL impairment observed among patients without any surgical history. This paradox likely represents a subgroup with advanced or non-operable malignancies, in whom uncontrolled tumor burden and cytokine release generate a pervasive inflammatory milieu. In such cases, the magnitude of systemic inflammation may override the modulatory influence of individual comorbidities, resulting in substantial psychosocial distress driven by chronic pruritus[2,3].

### Clinical Implications: Toward an Integrated Onco-Dermatology Approach

The robust association between NRS and DLQI validates itch intensity as a reliable surrogate marker of patient suffering. These findings support the proposal that chronic pruritus should be recognized as the "Fifth Vital Sign" in oncology practice, alongside pain, fatigue, and nutritional status[3]. Routine assessment using standardized patient-reported outcome measures such as the Numerical Rating Scale and Dermatology Life Quality Index may enable early identification of high-risk patients and facilitate timely, targeted interventions[4].

From a clinical perspective, cancer patients with endocrine or respiratory comorbidities—particularly hypothyroidism and asthma—should be proactively screened for refractory pruritus and considered for early multimodal management, including aggressive skin barrier repair and neuromodulatory therapy when indicated. The present findings further advocate for a collaborative Onco-Dermatology model, wherein dermatologists and oncologists work together to manage not only the malignancy but also the comorbidity-driven itch cycle that threatens treatment adherence and patient resilience[1–3,6].

### Regional Considerations

The study's setting in Udaipur, Rajasthan—a region characterized by hot and arid climatic conditions—may have further exacerbated xerosis and barrier dysfunction, particularly among patients with endocrine comorbidities. This environmental context adds a unique regional dimension to the findings and underscores the importance of climate-sensitive supportive care strategies in oncology patients with chronic pruritus[1,5].

### Limitations and Future Directions

The present study has certain limitations that should be considered while interpreting the findings. First, the cross-sectional design precludes the establishment of a temporal or causal relationship between chronic pruritus, comorbidities, and quality-of-life impairment. While a strong association between itch severity and QoL was observed, longitudinal studies are required to determine whether effective pruritus control leads to sustained improvement in psychosocial outcomes[1,3].

Second, the sample size was relatively modest (n = 85) and derived from a single tertiary care center, which may limit the generalizability of the findings to broader oncological populations. Multicentric studies with larger sample sizes would help validate the identified high-risk comorbidity phenotypes and strengthen external validity[2].

Third, although validated patient-reported outcome measures such as NRS and DLQI were employed, objective biomarkers of systemic inflammation or neuro-immune activation (e.g., cytokine profiles, serum bile acids, or nerve fiber density) were not assessed. Incorporation of such biomarkers in future studies could provide mechanistic insights into the neuro-immune pathways underlying the observed "double-hit" phenomenon[5,6].

Additionally, the study did not stratify patients based on type or stage of malignancy, oncological treatment modalities, or duration of cancer, all of which may independently influence pruritus severity and QoL impairment. Future research integrating oncological variables alongside dermatological and systemic factors would allow a more nuanced understanding of pruritus in cancer care[2,3].

### Future Directions

Future studies should adopt prospective longitudinal designs to evaluate the dynamic relationship between itch severity, comorbidity control, and quality-of-life outcomes over the course of cancer treatment. Interventional trials assessing targeted strategies—such as aggressive skin barrier repair in hypothyroid patients or immuno-modulatory approaches in asthmatic patients—may help establish evidence-based pruritus management protocols[1,5].

There is also a need to explore integrated Onco-Dermatology care models, wherein routine pruritus screening using standardized tools (NRS and DLQI) is incorporated into oncology clinics. Such models may improve early identification of refractory pruritus and enhance treatment adherence and patient resilience[3,4].

Finally, given the influence of regional climatic factors observed in this study, future research should consider environmental and geographical variables when evaluating chronic pruritus. Studies from diverse climatic zones could further elucidate the interaction between environmental xerosis, systemic comorbidities, and cancer-related inflammation in shaping pruritic burden[1,5].

## CONCLUSION

Chronic pruritus in cancer patients is a significant psychodermatological burden driven by the interaction between malignancy-related systemic inflammation and coexisting comorbidities. Endocrine and respiratory disorders, particularly hypothyroidism and asthma, markedly amplify itch severity and quality-of-life impairment. Routine assessment of pruritus using standardized patient-reported outcome measures and adoption of an integrated Onco-Dermatology approach are essential to improve holistic cancer care.