Stress as an exacerbating factor in chronic pruritus is associated with a distinct sensory phenotype and greater quality-of-life burden

Kadambari Ayithi, MS[1]; Elise Edwards, BA[1]; Kristen M. Sanders, PhD[1]; Leigh A. Nattkemper, PhD[1]; Emilie Fowler, MD[1]; Christina Kursewicz, BS[1]; and Gil Yosipovitch, MD[1]*

[1]Miami Itch Center and Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA

Psychological stress is frequently reported to exacerbate chronic pruritus, yet whether patients with stress-sensitive itch represent a clinically distinctive subgroup remains poorly characterized[1,2]. We aimed to identify clinically actionable markers by characterizing the sensory, clinical, and quality of life phenotype associated with stress-sensitive chronic pruritus. We conducted a cross-sectional analysis of adults with chronic pruritus presenting to dermatology clinics at Temple University and the University of Miami between 2015 and 2026. Patients were classified as stress-sensitive if they identified stress as an itch-exacerbating factor. Demographic characteristics, itch intensity, sensory qualities, additional exacerbating triggers, and itch-related quality of life (ItchyQoL)[3] were compared between stress-sensitive and stress-insensitive patients. Continuous and categorical variables were compared using Mann-Whitney U and chi-square tests respectively. Multivariable regression evaluated the independent association between stress sensitivity and ItchyQoL after adjustment for age, sex, diagnosis category, mood disorder, and psychiatric medication use.

Of 832 patients, 367 (44.1%) reported stress-related itch exacerbation. Median itch intensity was identical between stress-sensitive and stress-insensitive patients (NRS 7.0 vs 7.0; *P*=.720), yet substantial differences emerged in other dimensions of itch burden. Stress-sensitive patients

reported greater hurting, painful, burning, and stinging sensations (all $P<.001$) and were more likely to endorse every additional itch trigger assessed, with odds ratios ranging from 2.0 for hot water to 6.2 for contact allergens. Total ItchyQoL was substantially worse in stress-sensitive patients (median 78 vs 66; $P<.001$; rank-biserial $r=0.34$), with greater impairment across symptom, functioning, and emotional domains. This association persisted after adjustment for demographic and clinical covariates, with stress sensitivity independently associated with an 8.56-point higher Total ItchyQoL score (95% CI, 5.97–11.15; $P<.001$). Stress-sensitive patients were also younger (median 57 vs 65 years; $P<.001$) and more frequently female (66.5% vs 50.5%; $P<.001$).

Stress-sensitive chronic pruritus is associated with a substantially greater multidimensional disease burden that is not captured by itch intensity alone. Despite identical itch NRS scores, these patients experience more painful sensory qualities, broader trigger sensitivity, and greater quality-of-life impairment. Asking whether stress exacerbates itch may therefore provide a simple, clinically useful marker of patients whose disease burden is underestimated by conventional itch intensity measures and who warrant broader assessment of sensory, quality-of-life, and psychosocial dimensions. Prospective studies should determine whether stress-targeted interventions improve outcomes in this phenotype.

References:

1. Khalil NB, Coscarella G, Dhabhar FS, Yosipovitch G. A Narrative Review on Stress and Itch: What We Know and What We Would Like to Know. *J Clin Med*. 2024;13(22):6854. doi:10.3390/jcm13226854
2. Golpanian RS, Kim HS, Yosipovitch G. Effects of Stress on Itch. *Clin Ther*. 2020;42(5):745-756. doi:10.1016/j.clinthera.2020.01.025

3. Desai NS, Poindexter GB, Monthrope YM, Bendeck SE, Swerlick RA, Chen SC. A pilot quality-of-life instrument for pruritus. J Am Acad Dermatol. 2008;59(2):234-244. doi:10.1016/j.jaad.2008.04.006

Disclosures: Dr. Gil Yosipovitch serves as an advisory board member for Arcutis Biotherapeutics, AbbVie, Eli Lilly, Galderma, GSK, Kiniksa Pharmaceuticals, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc, Sanofi, Escient, and Merck Vifor. Dr. Gil Yosipovitch receives grants/research funding from Regeneron Pharmaceuticals, Inc and Sanofi. Dr. Gil Yosipovitch is an investigator for Pfizer, Eli Lilly, Novartis, Escient, and Sanofi. No other disclosures to report.