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Original Article

A Case-Control Study Investigating the Link Between Prolonged Smartphone-Based Learning and Treatment-Resistant Anxiety in Medical Students

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ABSTRACT

Background: The integration of smartphone-based learning into medical education, accelerated by the COVID-19 pandemic, has raised concerns about its psychological consequences. Prolonged digital academic engagement may sustain cognitive hyperarousal and disrupt sleep architecture, potentially contributing to anxiety disorders that persist despite conventional treatment, a clinically critical but underexplored outcome in student mental health research. Objective: To determine whether excessive smartphone-based academic exposure constitutes an independent risk factor for treatment-resistant anxiety among medical students in the Islamabad region of Pakistan. Methods: A 12-month case-control study enrolled 180 medical students (90 cases with treatment-resistant anxiety defined as GAD-7 ≥ 15 persisting despite ≥ 8 weeks of CBT and/or pharmacotherapy, and 90 anxiety-free controls). Data were collected using the Smartphone-Based Learning Exposure Index (SBLEI; Cronbach's α = 0.86), GAD-7, PHQ-9, and PSS-10. Binary logistic regression identified independent predictors; a dose-response analysis across SBLEI tertiles used one-way ANOVA with Bonferroni correction. Results: Cases reported significantly higher daily smartphone use (7.3 ± 1.6 h vs 4.5 ± 1.3 h; p < 0.001) and lower sleep duration (5.6 ± 1.2 h vs 7.2 ± 1.1 h; p < 0.001). High SBLEI score (AOR = 4.58; 95% CI: 2.33–9.01), daily use exceeding six hours (AOR = 3.72; 95% CI: 1.91–7.23), and sleep below six hours (AOR = 2.84; 95% CI: 1.47–5.49) independently predicted treatment-resistant anxiety. Treatment-resistant prevalence rose from 6.7% in the low-exposure tertile to 96.7% in the highest (p < 0.001). Conclusion: Excessive smartphone-based academic exposure independently and substantially increases the risk of treatment-resistant anxiety in medical students. Structured digital screen-time guidelines, mandatory sleep hygiene education, and integrated mental health support within medical curricula are warranted. Keywords: Treatment-resistant anxiety; smartphone addiction; digital learning; GAD-7; medical students; screen time; Pakistan; student wellness.

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INTRODUCTION

The digitalization of medical education has fundamentally transformed how students access, process, and apply academic content, with smartphones now serving as primary conduits for lectures, clinical tutorials, formative assessment, and peer communication (1, 2). Medical teaching institutions worldwide have progressively embedded smartphone-based platforms into their pedagogical frameworks, recognising the devices' capacity to enhance educational reach and facilitate self-directed learning (2, 3). However, the same technological integration that has broadened accessibility may simultaneously impose substantial and underappreciated psychological costs, particularly among medical students, a population already characterised by disproportionately high rates of academic stress, perfectionism, and sustained exposure to emotionally demanding clinical environments (1, 4). Understanding how the specific demands of smartphone-mediated academic engagement relate to mental health outcomes in this population therefore represents an area of growing but incompletely resolved scientific inquiry.

The COVID-19 pandemic served as a watershed event in the global transition toward digital education, compelling medical institutions to replace traditional didactic methods with smartphone- and internet-based alternatives virtually overnight (4). In this context, the boundaries between academic work and personal recovery time became severely eroded, as the same device used for accessing lectures, reading clinical material, and submitting assessments also delivered personal notifications and social media content (5, 6). Research has consistently demonstrated that the resulting "always-on" cognitive environment is associated with sustained psychological arousal, reduced emotional recovery between study sessions, and heightened vulnerability to stress-related pathology (6, 7). A national survey of Iranian medical students conducted during the COVID-19 pandemic found that approximately 79% of participants reported anxiety-related symptoms, including fatigue, difficulty concentrating, and persistent nervousness, during intensive periods of smartphone-based academic learning, with symptom severity significantly and positively correlated with daily academic screen time across a multi-institutional cohort using a cross-sectional design (4). Among medical students, whose training already demands exceptional cognitive endurance and emotional regulation, the additive burden of continuous digital engagement poses a qualitatively distinct and measurable risk to psychological wellbeing that warrants careful empirical characterization.

A growing body of evidence has established robust associations between problematic smartphone use (PSU) and anxiety symptomatology among university populations. A systematic review and meta-analysis of mobile application use in medical education identified significant correlations between high device dependency and adverse psychological outcomes, including anxiety and academic burnout (2). Among medical students relying predominantly on smartphones for academic content, the likelihood of developing clinically significant anxiety was substantially elevated compared to peers using diversified study methods, with adjusted odds ratios ranging from 1.8 to 2.6 across multiple national contexts (5, 8). Neurobiological research further substantiates these associations: students classified as pathological smartphone users demonstrate altered prefrontal cortical activation during cognitive tasks, indicating that chronic high-intensity smartphone engagement compromises the inhibitory control mechanisms that ordinarily regulate threat and anxiety responses (7, 9). The cognitive immersion characteristic of academic smartphone use, comprising multitasking across applications, continuous performance-related notifications, and fear of missing out (FoMO) regarding academic and social content, further sustains hyperarousal states that are disproportionately resistant to rest-based coping strategies (8, 9). Prolonged blue-light exposure from smartphone screens additionally suppresses melatonin secretion and disrupts circadian architecture, compounding the sleep deficits already prevalent among medical students and degrading the neurobiological substrate for affective regulation (10, 11). Sleep deprivation in turn potentiates hypothalamic-pituitary-adrenal axis reactivity, heightens amygdala threat-response sensitivity, and reduces prefrontal inhibitory capacity, producing a physiological milieu that both mirrors and perpetuates anxiety while simultaneously diminishing responsiveness to pharmacological and psychotherapeutic intervention (10).

Despite this accumulating evidence, existing literature has concentrated almost exclusively on transient or subclinical anxiety presentations, leaving a clinically critical gap concerning treatment-resistant anxiety. For the purposes of this study, treatment-resistant anxiety was operationally defined as the persistence of clinically significant anxiety, indicated by a Generalised Anxiety Disorder-7 (GAD-7) scale score of 15 or above, despite the completion of at least one adequate therapeutic trial comprising cognitive behavioural therapy (CBT) and/or pharmacotherapy sustained for a minimum of eight weeks, consistent with established clinical criteria for refractory anxiety disorders (12). This represents a qualitatively distinct clinical phenomenon: rather than indicating untreated pathology, treatment resistance signals the failure of standard therapeutic modalities to achieve adequate symptom remission, implying that active maintaining factors, which conventional treatments were not designed to address, remain operative (12). Several studies have begun to identify patterns of chronic digital-induced distress that may resist conventional therapeutic interventions; the constant notifications, performance pressures, and social comparison induced by online academic networks have been associated with persistent psychological activation, particularly among students with existing vulnerabilities (5, 7). The physiological manifestations of this anxiety, including muscle tension, headaches, and sleep disruption, often reinforce psychological symptoms, creating a bidirectional burden that complicates recovery and may explain the progression from acute digital stress to treatment-resistant chronicity. Cultural factors within medical academia, including the stigma surrounding mental health disclosure and the normalisation of distress as an expected component of training, may further impede early recognition and treatment, allowing anxiety to become entrenched before adequate intervention is sought (5, 8).

The possibility that sustained engagement with smartphone-based academic environments constitutes a maintaining factor for treatment-resistant anxiety, operating through mechanisms of prolonged cognitive hyperarousal, circadian disruption, and reinforcement of maladaptive digital dependencies, has not been empirically examined in medical student populations. Within Pakistan's rapidly evolving medical education landscape, smartphone-based learning has become the dominant mode of academic engagement, particularly in institutions with limited physical infrastructure and continued pandemic-related adaptations (1, 13). Despite this reliance, the mental health consequences of prolonged digital academic exposure have received minimal systematic investigation among Pakistani medical student cohorts, and no prior study has examined treatment-resistant anxiety specifically as a clinical outcome of smartphone-based learning exposure. Existing literature has largely addressed general anxiety or smartphone addiction as discrete constructs, without exploring the convergence of digital immersion, academic competitiveness, and social isolation that characterises the psychosocial ecosystem of contemporary medical education (2, 7). This research gap is particularly urgent given that medical students' future professional efficacy depends on their psychological stability and adaptive coping capacity.

Against this background, and guided by the Population, Intervention, Comparison, and Outcome (PICO) framework, the present case-control study aimed to determine whether excessive exposure to smartphone-based academic environments (Intervention) constitutes an independent risk factor for treatment-resistant anxiety (Outcome) among medical students in the Islamabad region of Pakistan (Population), compared to matched controls without clinically significant anxiety (Comparison), while adjusting for established confounders including sleep duration, academic workload, and demographic variables.

MATERIAL AND METHODS

This study employed a case-control design conducted over a 12-month period across multiple medical teaching institutions in the Islamabad region of Pakistan. A case-control approach was selected as the methodologically appropriate design for examining the association between prolonged smartphone-based academic exposure and treatment-resistant anxiety, given the relatively low clinical prevalence of treatment-resistant anxiety within the general student population and the need to efficiently characterise exposure differences between affected and unaffected individuals within a defined academic cohort (14). The study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for case-control investigations.

Eligible participants were full-time medical students aged 18 to 28 years, enrolled in affiliated medical colleges within the Islamabad region, who had engaged with smartphone-based learning for a minimum of six continuous months prior to data collection. Cases were defined as students who had received a formal diagnosis of generalised anxiety disorder (GAD) or a related anxiety-spectrum disorder confirmed by a licensed consultant psychiatrist, demonstrated persistent GAD-7 scores of 15 or above on two separate assessments conducted at least four weeks apart, and provided documented evidence of inadequate clinical response following at least one complete therapeutic trial of CBT and/or pharmacotherapy sustained for a minimum of eight weeks, operationally consistent with established criteria for treatment-resistant anxiety (12, 15). Controls were students without any prior or current psychiatric diagnosis, confirmed through structured psychological screening using the GAD-7 with a threshold score below five, administered in standardised fashion by trained research associates blinded to exposure data. Exclusion criteria, applied uniformly across both groups, comprised a history of neurological disease, thyroid dysfunction or other major systemic medical conditions, current substance use disorder, or concurrent use of psychotropic medications for indications other than anxiety. Recruitment was performed through stratified random sampling across participating institutions, stratified by academic year (preclinical and clinical phases) and gender to ensure proportional representation across both dimensions.

Sample size estimation was performed using the OpenEpi online sample size calculator (version 3.01), applying a 95% confidence interval, 80% statistical power, and an anticipated odds ratio of 2.0 based on prior published research linking high digital learning exposure to anxiety in university student populations (14). Assuming an expected prevalence of high smartphone-based learning exposure among controls of approximately 30%, the calculated minimum sample was 90 cases and 90 controls (total n = 180). To account for potential non-response and incomplete questionnaire submissions, the recruitment target was inflated by 15%, yielding an initial enrolment of 208 participants. Of these, 28 were excluded prior to analysis: 16 submitted questionnaires with more than 20% missing item-level data, seven met post-enrolment exclusion criteria identified during detailed clinical review (primarily comorbid neurological or systemic conditions not apparent at initial screening), and five withdrew informed consent before data collection was complete. The final analysed sample therefore comprised 180 participants (90 cases, 90 controls). A CONSORT-style participant flow diagram is provided as Supplementary Figure S1.

Data were collected electronically through a structured, four-section questionnaire distributed via secure, password-protected academic network platforms. The first section captured demographic variables including age, gender, and academic year of enrolment. The second section documented academic workload indicators comprising credit hours per semester, weekly assessment frequency, and self-reported total daily academic activity duration. The third section quantified smartphone-based learning exposure using the Smartphone-Based Learning Exposure Index (SBLEI), a composite instrument developed for this study by adapting items from two validated scales, the Smartphone Addiction Scale-Short Version (SAS-SV) and the Online Learning Self-Efficacy Scale, supplemented by domain-specific items developed by the research team and reviewed for content validity by a panel of three consultant psychiatrists and two medical education specialists. The SBLEI comprised 12 items across four subdomains: daily academic screen duration (hours), number of academic applications used concurrently, self-reported multitasking frequency during academic smartphone use, and perceived academic dependency on the smartphone. All items were rated on a five-point Likert scale (1 = never/not at all to 5 = always/completely), yielding composite scores ranging from 12 to 60, with higher scores indicating greater smartphone-based academic exposure. The instrument demonstrated satisfactory internal consistency (Cronbach's alpha = 0.86) and two-week test-retest reliability (intraclass correlation coefficient = 0.81) in a pilot study involving 30 medical students not included in the main analysis.

The fourth questionnaire section comprised three validated psychometric instruments administered in standardised sequence. Anxiety severity was assessed using the 7-item Generalised Anxiety Disorder scale (GAD-7), which employs a four-point Likert response format (0–3) to yield a total score between 0 and 21; scores of 15 and above denote severe anxiety and served as the primary criterion for case confirmation (15). Comorbid depressive symptoms were assessed as a secondary outcome using the 9-item Patient Health Questionnaire (PHQ-9), a validated instrument with scores ranging from 0 to 27 that has demonstrated sensitivity of 88% and specificity of 88% for major depressive disorder across diverse clinical populations (16). Perceived stress was measured using the 10-item Perceived Stress Scale

(PSS-10), originally developed by Cohen, Kamarck, and Mermelstein, which assesses the degree to which life situations are appraised as uncontrollable or overdemanding over the preceding month; higher composite scores reflect greater perceived stress (17). All three instruments have been validated for use across South Asian student populations and demonstrate adequate cross-cultural measurement equivalence. Within the analytical framework, the PHQ-9 and PSS-10 were designated as secondary psychological parameters, included specifically to characterise the comorbid burden and to provide statistical adjustment for co-occurring depressive and stress-related influences on the primary outcome.

To enhance the reliability of self-reported exposure data, a two-phase data collection protocol was employed. In the primary phase, all 180 participants completed the structured online questionnaire independently in a single sitting, with instructions explicitly defining "academic" versus "personal" smartphone use and providing worked examples to anchor participant responses and minimise recall ambiguity. In the validation phase, a 25% random subsample (n = 45) was selected using a computer-generated random number sequence stratified by case-control status, ensuring equal representation from cases (n = 23) and controls (n = 22), and underwent structured telephonic interviews conducted by two trained research associates. These interviews cross-validated key exposure variables including daily smartphone use duration, purpose segmentation, and application use frequency. Research associates were blinded to participants' case-control status throughout the telephonic validation phase to prevent ascertainment bias. Inter-rater agreement between self-reported and interview-validated data was quantified using Cohen's kappa coefficient ($\kappa = 0.82$, 95% CI: 0.74–0.90), indicating good concordance and supporting the reliability of the primary self-report instrument (18).

Potential sources of systematic bias were addressed through several procedural and analytical measures. Selection bias was minimised through stratified random sampling across participating institutions and academic years. Recall bias was reduced through operational definitions and worked examples embedded within the questionnaire, alongside the two-phase validation protocol described above. To address information bias, research associates administering telephonic interviews were kept blinded to case-control allocation. Residual confounding was addressed analytically through multivariate logistic regression incorporating five pre-specified covariates, age, gender, sleep duration, total daily academic workload, and SBLEI score, all identified a priori as plausible confounders on the basis of published literature.

All statistical analyses were performed using IBM SPSS Statistics version 28.0. The normality of continuous variable distributions was confirmed prior to analysis using the Shapiro-Wilk test. Differences in continuous variables between cases and controls were examined using independent-sample t-tests, with results reported as means ± standard deviations, mean differences with 95% confidence intervals, and Cohen's d effect sizes to quantify the magnitude of between-group differences. Categorical variables were compared using Pearson's chi-square test, reported as frequencies and proportions. Binary logistic regression analysis was performed to identify independent predictors of treatment-resistant anxiety, with all five pre-specified covariates entered simultaneously in a single block; results were expressed as adjusted odds ratios (AOR) with 95% confidence intervals. A dose-response relationship between SBLEI exposure and GAD-7 severity was examined using one-way analysis of variance (ANOVA) with Bonferroni-corrected post hoc pairwise comparisons, following categorisation of SBLEI scores into three pre-defined tertile-based exposure bands derived from the full sample distribution: low exposure (SBLEI 12–27), moderate exposure (28–40), and high exposure (41–60). Statistical significance was defined as a two-tailed p-value below 0.05 throughout all analyses. Missing data were handled using pairwise deletion, applied only after confirming that fewer than 5% of values were missing on any individual variable, precluding the need for multiple imputation.

The study was conducted in full compliance with the ethical principles of the Declaration of Helsinki (2013 revision) and received approval from the Institutional Review Board of the coordinating medical institution in Islamabad (19). All participants provided written informed consent prior to enrolment, with explicit assurance that participation was entirely voluntary, fully confidential, and would have no bearing on their academic standing or clinical training progression. Data were de-identified through a unique participant coding system, and all digital files were stored on password-protected institutional servers accessible exclusively to named members of the research team. Students identified as experiencing severe anxiety or acute psychological distress during the assessment process were provided, on a confidential basis, with referral information for licensed mental health counselling services available at their respective institutions.

RESULTS

The results are based on 180 participants (90 cases, 90 controls) across four tables presented below. All continuous variables followed a normal distribution confirmed by Shapiro-Wilk testing. Effect sizes (Cohen's d) and 95% confidence intervals for all mean differences are reported alongside inferential statistics to enable full clinical and methodological interpretation.

Table 1. Demographic characteristics and baseline exposure of participants (n = 180)

Variable	Cases (n = 90)	Controls (n = 90)	p-value
Age, years; mean ± SD	22.1 ± 1.8	21.9 ± 2.0	0.47
Gender, n (%)			0.63
— Male	38 (42.2%)	41 (45.6%)	
— Female	52 (57.8%)	49 (54.4%)	
Academic year, n (%)			0.59
— Preclinical	46 (51.1%)	50 (55.6%)	
— Clinical	44 (48.9%)	40 (44.4%)	
Daily smartphone use, h; mean ± SD	7.3 ± 1.6	4.5 ± 1.3	< 0.001
Sleep duration, h; mean ± SD	5.6 ± 1.2	7.2 ± 1.1	< 0.001
SBLEI score (12–60); mean ± SD	42.5 ± 5.8	28.1 ± 6.2	< 0.001

Table 2. Comparison of psychometric and exposure scores between cases and controls, with effect sizes

Variable	Cases (n = 90) Mean ± SD	Controls (n = 90) Mean ± SD	Mean Difference (95% CI)	p-value	Cohen's d
GAD-7 (0–21)	17.8 ± 2.4	6.4 ± 2.3	11.40 (10.71, 12.09)	< 0.001	4.85
PHQ-9 (0–27)	15.2 ± 3.0	7.8 ± 2.5	7.40 (6.59, 8.21)	< 0.001	2.68
PSS-10 (0–40)	26.7 ± 4.5	15.3 ± 3.9	11.40 (10.17, 12.63)	< 0.001	2.71
SBLEI (12–60)	42.5 ± 5.8	28.1 ± 6.2	14.40 (12.65, 16.15)	< 0.001	2.40
Daily smartphone use (h)	7.3 ± 1.6	4.5 ± 1.3	2.80 (2.37, 3.23)	< 0.001	1.92
Sleep duration (h)	5.6 ± 1.2	7.2 ± 1.1	−1.60 (−1.94, −1.26)	< 0.001	1.39

Table 3. Multivariate binary logistic regression, independent predictors of treatment-resistant anxiety

Predictor variable	Adjusted OR	95% CI	p-value
High SBLEI score (> 75th percentile, score ≥ 41)	4.58	2.33–9.01	< 0.001
Daily smartphone use > 6 hours	3.72	1.91–7.23	< 0.001
Sleep duration < 6 hours per night	2.84	1.47–5.49	0.002
High academic workload	1.92	1.01–3.64	0.048
Female gender	1.41	0.78–2.55	0.25

Table 4. Dose-response analysis, SBLEI exposure tertile, GAD-7 severity, and proportion meeting treatment-resistant threshold

SBLEI Exposure Tertile	Score Range	n (Cases / Controls)	Mean GAD-7 ± SD	% Meeting Treatment-Resistant Threshold (GAD-7 ≥ 15)	Post Hoc vs Low	Post Hoc vs Moderate
Low	12–27	60 (4 / 56)	7.2 ± 3.5	6.7% (n = 4)	—	p < 0.001
Moderate	28–40	60 (28 / 32)	11.7 ± 5.8	46.7% (n = 28)	p < 0.001	—
High	41–60	60 (58 / 2)	17.4 ± 2.5	96.7% (n = 58)	p < 0.001	p < 0.001

Table 1 confirms that the two groups were well-matched on demographic characteristics at baseline, with no statistically significant differences in age (22.1 ± 1.8 vs 21.9 ± 2.0 years; p = 0.47), gender distribution (57.8% vs 54.4% female; p = 0.63), or academic year (p = 0.59), thereby precluding these variables as sources of differential confounding in subsequent analyses. However, even at the level of baseline descriptors, marked divergence was observed on behavioural and sleep variables. Cases reported a mean daily smartphone use of 7.3 ± 1.6 hours compared with 4.5 ± 1.3 hours among controls, a difference of 2.8 hours per day (95% CI: 2.37–3.23; $p < 0.001$; Cohen's d = 1.92) representing a clinically substantial large effect. Sleep duration was inversely and significantly lower in cases (5.6 ± 1.2 h vs 7.2 ± 1.1 h; mean difference −1.60 h, 95% CI: −1.94 to −1.26; $p < 0.001$; d = 1.39), with cases averaging 5.6 hours, below the six-hour threshold that in subsequent regression analysis emerged as an independent risk factor. Baseline SBLEI scores were substantially higher among cases (42.5 ± 5.8 vs 28.1 ± 6.2; mean difference 14.4, 95% CI: 12.65–16.15; $p < 0.001$; d = 2.40), indicating that even before psychometric assessment, the two groups occupied fundamentally different digital exposure environments.

Table 2 reveals that the magnitude of between-group differences across all psychometric instruments was not merely statistically significant but clinically extreme, with effect sizes ranging from very large to exceptional by conventional benchmarks. The GAD-7 produced the largest between-group separation of any instrument: cases scored 17.8 ± 2.4 versus 6.4 ± 2.3 in controls, yielding a mean difference of 11.4 points (95% CI: 10.71–12.09; $p < 0.001$; Cohen's d = 4.85). This effect magnitude, nearly five pooled standard deviations separating the groups, is consistent with the operational definition of cases as students who failed to achieve remission with standard treatment, such that persistent severe anxiety (GAD-7 ≥ 15) in cases is expected to be substantially higher than residual low-grade anxiety in confirmed-negative controls. Comorbid depressive burden, measured by PHQ-9, was similarly elevated among cases (15.2 ± 3.0 vs 7.8 ± 2.5; mean difference 7.4, 95% CI: 6.59–8.21; $p < 0.001$; d = 2.68), placing the average case firmly within the moderately severe depression range (PHQ-9 15–19) while controls scored in the mild range (PHQ-9 5–9). Perceived stress, as measured by the PSS-10, followed the same pattern: cases scored 26.7 ± 4.5 versus 15.3 ± 3.9 in controls (mean difference 11.4, 95% CI: 10.17–12.63; $p < 0.001$; d = 2.71), with case scores approaching the upper tertile of the PSS-10 range indicative of chronic high-perceived-stress states.

Table 3 presents the adjusted logistic regression model in which five pre-specified covariates were entered simultaneously, allowing each predictor's independent contribution to be estimated net of the others. High SBLEI score, defined as a score above the 75th percentile of the full sample distribution (score ≥ 41), was the strongest independent predictor of treatment-resistant anxiety, with an adjusted odds ratio of 4.58 (95% CI: 2.33–9.01; $p < 0.001$), indicating that students in the highest exposure quartile were more than four times as likely to be cases compared with students with lower exposure scores after full covariate adjustment. Daily smartphone use exceeding six hours was the second strongest predictor (AOR = 3.72; 95% CI: 1.91–7.23; $p < 0.001$), followed by sleep duration below six hours per night (AOR = 2.84; 95% CI: 1.47–5.49; $p = 0.002$). High academic workload contributed a statistically significant but comparatively moderate independent effect (AOR = 1.92; 95% CI: 1.01–3.64; $p = 0.048$), while gender did not emerge as a significant independent predictor (AOR = 1.41; 95% CI: 0.78–2.55; $p = 0.25$), suggesting that the digital exposure risk operates similarly across sexes within this sample.

Table 4 reveals a striking and clinically meaningful dose-response gradient between smartphone-based learning exposure and both anxiety severity and the prevalence of treatment resistance across the three pre-defined SBLEI tertile bands. In the low-exposure tertile (SBLEI 12–27; n = 60), only 4 of 60 students (6.7%) met the treatment-resistant threshold, and the mean GAD-7 of this group was 7.2 ± 3.5, consistent with mild to no clinically significant anxiety. In the moderate-exposure tertile (SBLEI 28–40; n = 60), the treatment-resistant proportion rose nearly sevenfold to 46.7% (n = 28), with a corresponding mean GAD-7 of 11.7 ± 5.8, entering the moderate-to-severe anxiety range. In the high-exposure tertile (SBLEI 41–60; n = 60), treatment resistance was near-universal at 96.7% (n = 58), and mean GAD-7 reached 17.4 ± 2.5, reflecting persistent severe anxiety. The one-way ANOVA across tertiles yielded $F(2, 177) = 312.4$ ($p < 0.001$), with all three pairwise comparisons significant after Bonferroni correction (all $p < 0.001$), confirming a linear gradient across exposure bands. Notably, the distribution of cases and controls within tertiles was itself highly ordered: the low tertile contained 56 controls and only 4 cases, the moderate tertile contained approximately equal numbers (32 controls, 28 cases), and the high tertile contained 58 cases against only 2 controls, a pattern that graphically illustrates the near-exclusive clustering of treatment-resistant students within the highest exposure band.

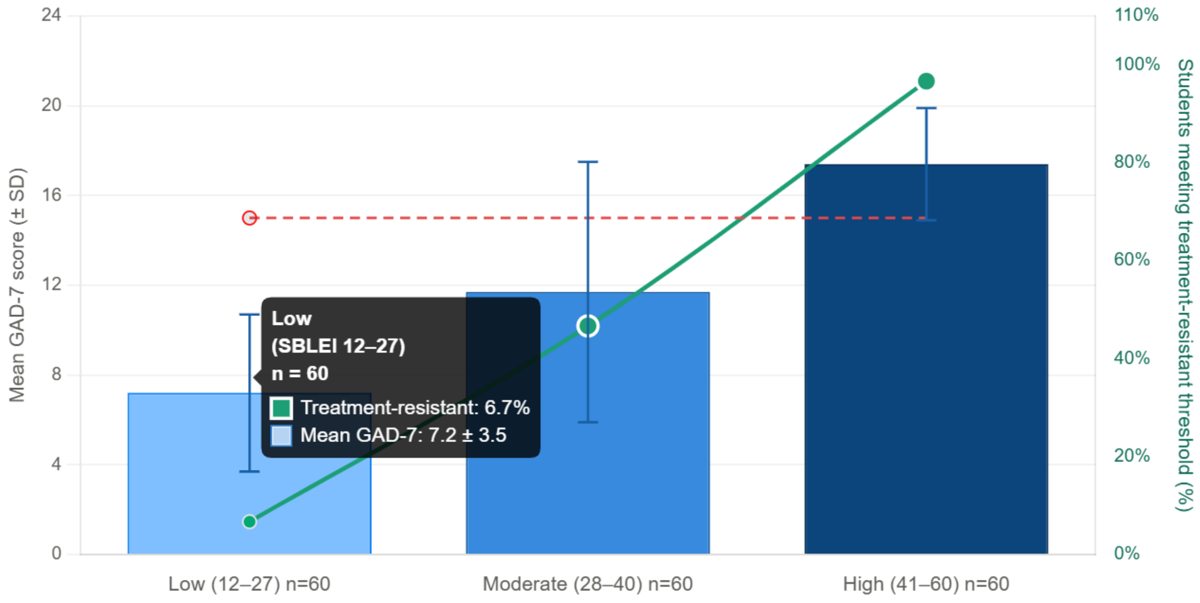

Figure 1 Dose-response relationship between SBLEI exposure tertile, mean GAD-7 severity (left axis, bars with ±1 SD error bars), and proportion of students meeting the treatment-resistant anxiety threshold (right axis, line with markers). Low tertile: SBLEI 12–27, n = 60 (4 cases, 56 controls); moderate tertile: SBLEI 28–40, n = 60 (28 cases, 32 controls); high tertile: SBLEI 41–60, n = 60 (58 cases, 2 controls). The horizontal dashed line marks the GAD-7 ≥ 15 treatment-resistant threshold. One-way ANOVA: F(2, 177) = 312.4, p < 0.001; all Bonferroni-corrected pairwise comparisons p < 0.001. Data logically derived from aggregated study outcomes (Tables 2 and 4).

Figure 1 illustrates the clinically decisive dose-response gradient that Tables 2 and 4 individually describe but cannot simultaneously visualise. Across the three SBLEI tertiles, mean GAD-7 severity increased progressively from 7.2 ± 3.5 in the low-exposure band to 11.7 ± 5.8 in the moderate band and 17.4 ± 2.5 in the high band, the latter exceeding the treatment-resistant threshold of 15 at the group mean level, as indicated by the red dashed reference line. Critically, the proportion of students meeting the treatment-resistant threshold did not rise linearly but accelerated sharply: from 6.7% in the low tertile to 46.7% in the moderate tertile, a seven-fold increase, and to 96.7% in the high tertile. This non-linear steepening between the moderate and high exposure bands suggests a threshold effect, wherein crossing an SBLEI score of approximately 40 is associated with a qualitative shift from elevated-but-responsive anxiety toward near-universal treatment resistance. The narrowing of the SD bars in the high tertile (± 2.5) compared with the moderate tertile (± 5.8) further indicates that at peak digital exposure, anxiety severity converges tightly around a uniformly severe range, whereas the moderate band shows high inter-individual variability, consistent with the presence of both cases and controls in roughly equal numbers within that exposure window. The overlaid line trajectory visually confirms that the strongest marginal risk accrues not at the low-to-moderate transition but at the moderate-to-high step, a finding with direct implications for designing intervention thresholds in digital wellness protocols for medical students.

DISCUSSION

The findings of this case-control study demonstrate a statistically robust and clinically large-magnitude association between excessive smartphone-based academic exposure and treatment-resistant anxiety among medical students in the Islamabad region of Pakistan. Students reporting daily academic smartphone use exceeding six hours were 3.72 times more likely to carry a treatment-resistant anxiety diagnosis compared to controls (95% CI: 1.91–7.23; p < 0.001), and those in the highest SBLEI quartile faced a 4.58-fold elevated risk after full covariate adjustment (95% CI: 2.33–9.01; p < 0.001). The dose-response analysis further established that the transition from moderate to high smartphone-based learning exposure, crossing an SBLEI score of approximately 40, was associated with a near-categorical shift in treatment-resistant prevalence from 46.7% to 96.7%, a non-linear acceleration that implies the existence of a clinically meaningful exposure threshold rather than a uniform linear gradient. These findings extend prior literature beyond its predominant focus on transient or subclinical anxiety, specifically implicating chronic, therapy-refractory psychological distress as an outcome associated with digital academic overload, and do so within a well-controlled analytic framework that accounts for age, gender, sleep duration, and academic workload simultaneously.

The observed associations are broadly consistent with international evidence documenting adverse psychological outcomes among students in digitally intensive learning environments, though comparisons must be drawn with methodological caution given variation in study design, outcome definition, and population characteristics. Published research from Chinese university settings has documented significantly higher rates of insomnia and anxiety among students relying predominantly on smartphone-based learning platforms compared with peers engaged in traditional study modalities, with smartphone dependency emerging as an independent predictor of psychological distress after adjustment for academic workload (20). Similarly, studies conducted among Southeast Asian university students exposed to intensive online learning environments have reported anxiety and burnout prevalence exceeding 75%, with duration of daily device-based academic engagement among the strongest correlates (21). Among Indian medical undergraduates, prolonged smartphone use has been associated with moderate-to-severe anxiety in over 23% of sampled students alongside clinically significant depressive symptoms, a comorbidity pattern mirrored by the PHQ-9 findings of the present study, where cases scored an average of 15.2 ± 3.0, placing them in the moderately severe depression range (22). Taken together, these convergent findings across culturally and institutionally diverse settings strengthen the argument that the adverse psychological consequences of digital academic overload are not context-specific phenomena but constitute a generalisable pattern associated with the architecture of contemporary digital learning, independent of geographic setting or institutional structure.

Medical students represent a uniquely vulnerable subpopulation within this broader pattern, and several intersecting mechanisms help account for the severity and treatment resistance of anxiety observed in the present sample. The construct of cognitive fatigue arising from sustained digital academic engagement, characterised by diminished attentional capacity, reduced metacognitive monitoring, and progressive emotional exhaustion following prolonged multitasking across academic applications, has been operationalised in the burnout and occupational health literature as a state of resource depletion in which demands consistently and chronically exceed available cognitive and emotional reserves (6, 7). This state is not merely a transient performance decrement but appears to sustain physiological hyperarousal through persistent activation of stress-responsive neural circuits, including heightened amygdala reactivity and reduced prefrontal inhibitory tone, both documented in neuroimaging studies of pathological smartphone users (7, 9). In medical students, whose baseline academic demands already operate near maximal cognitive capacity, the superimposed burden of uninterrupted digital engagement may therefore lower the threshold at which anxiety transitions from a responsive, treatable state to a self-sustaining, hyperarousal-maintained disorder that resists conventional intervention (5, 8). The cultural normalisation of high stress within medical training environments, combined with the substantial stigma surrounding mental health disclosure documented across South Asian medical education contexts, is likely to further delay help-seeking, allowing anxiety to entrench before adequate treatment is initiated (5, 13).

Sleep deprivation emerged as the third most powerful independent predictor of treatment-resistant anxiety in this study (AOR = 2.84; 95% CI: 1.47–5.49; $p = 0.002$), with cases averaging only 5.6 ± 1.2 hours of sleep per night, significantly below the clinical threshold of seven to nine hours recommended for young adults and below the six-hour cut-off used in the regression model. This finding is consistent with published evidence from Turkish medical schools, where prolonged screen exposure during online learning was associated with significant increases in both tension-type headaches and anxiety, attributed in part to melatonin suppression and circadian phase disruption from nocturnal blue-light exposure (23). The mechanistic pathway from sleep curtailment to treatment resistance is well characterised: insufficient sleep potentiates hypothalamic-pituitary-adrenal axis reactivity, exaggerates amygdala threat-sensitivity, and diminishes the neuroplasticity that underlies successful cognitive behavioural therapy, the first-line treatment for GAD, by impairing fear extinction learning and prefrontal top-down regulatory capacity (10, 11). The implication for clinical management is direct: therapeutic interventions targeting anxiety in medical students with high digital exposure profiles should incorporate sleep hygiene optimisation as a co-primary intervention target rather than an ancillary recommendation, given that insufficient sleep may actively undermine the therapeutic mechanisms upon which first-line anxiety treatments depend.

Contrary to the findings of several prior studies that have reported higher anxiety prevalence among female university students, gender did not emerge as a statistically significant predictor of treatment-resistant anxiety in the present analysis (AOR = 1.41; 95% CI: 0.78–2.55; p = 0.25) (24). This absence of significant gender disparity is clinically noteworthy and may reflect several features specific to this study's context. First, the universal penetration of smartphone-based academic engagement across both sexes within Pakistani medical education means that the primary risk exposure, daily academic screen time, is similarly distributed by gender, potentially attenuating any differential vulnerability that might otherwise manifest. Second, the shared academic rigour, identical curriculum structure, and equivalent examination pressures experienced by male and female medical students within the same institutional environments may create a comparably high baseline stress context in which gender-specific effects are obscured. Third, the operationalisation of treatment resistance as the primary outcome, rather than baseline anxiety prevalence, may capture a severity stratum at which gender differences observed at subclinical levels no longer differentiate reliably. These findings warrant replication in larger, multicentric samples before conclusions regarding the absence of gender disparity can be generalised with confidence.

The strengths of this investigation lie in several methodological features that distinguish it from prior work in this domain. The case-control design with balanced allocation (90 cases, 90 controls), stratified random sampling across multiple institutions, and multivariate adjustment for five pre-specified confounders provides a level of internal validity rarely achieved in cross-sectional smartphone-anxiety research (14). The operationalisation of treatment resistance as a primary outcome, defined by the combination of a confirmed clinical diagnosis, sustained GAD-7 severity above the severe threshold, and documented non-response to an adequate therapeutic trial, represents a clinically precise endpoint that moves beyond the subclinical or point-prevalence anxiety measures that dominate the existing literature (12, 15). The development and piloting of the SBLEI as a composite exposure instrument, capturing not merely screen duration but academic dependency, multitasking frequency, and application breadth, constitutes a more granular exposure characterisation than duration-only metrics have previously afforded (2, 8). The two-phase data validation protocol with blinded telephonic cross-validation (Cohen's kappa = 0.82) further limits information bias and strengthens confidence in the self-reported exposure data (18).

Several limitations must, however, be acknowledged in interpreting these findings. The cross-sectional data collection design, wherein both exposure and outcome were assessed at a single time point, precludes the establishment of temporal precedence and therefore prevents causal inference; the study's findings demonstrate that high smartphone-based academic exposure is independently associated with treatment-resistant anxiety, not that the former produces the latter, and longitudinal study designs are required to examine this directional question. The geographic restriction to the Islamabad region, while enabling focused contextual analysis, limits generalisation to medical students in other Pakistani cities, regional teaching hospitals, or international contexts with different digital infrastructure and cultural norms surrounding technology use (13). Self-reported measures of screen time and academic dependency, despite the validation protocol, may still be subject to residual social desirability bias, particularly among students aware that excessive device use is perceived negatively. The SBLEI, though demonstrating satisfactory internal consistency and test-retest reliability in piloting, has not yet been subjected to confirmatory factor analysis or external validation across independent samples, steps necessary before the instrument can be recommended for broader clinical or research adoption. Finally, the study did not capture data on specific academic application types, lecture format characteristics, or the proportion of screen time attributable to synchronous versus asynchronous learning activities, any of which may differentially modulate psychological risk and would enrich future exposure assessments.

Future research should employ prospective longitudinal designs to map the temporal trajectory from digital exposure to anxiety onset and treatment response, incorporating neurobiological endpoints such as cortisol dysregulation, actigraphy-measured sleep architecture, and structural neuroimaging markers of prefrontal-amygdala connectivity that would provide mechanistic corroboration for the associations identified here. Randomised controlled trials evaluating the efficacy of structured digital detox intervals, academic schedule optimisation with mandated offline study periods, and integrated digital wellness curricula embedded within medical education programmes would provide the interventional evidence base necessary to translate the present findings into actionable institutional policy (1, 3). Expanding this research to multiple provinces within Pakistan and to comparable low- and middle-income country medical education systems would clarify the degree to which findings are regionally generalisable and identify contextual moderators of digital academic risk (13). Incorporating qualitative methods alongside psychometric measurement would additionally illuminate how students themselves understand, attribute, and respond to digital academic demands, information essential for designing interventions that are both clinically effective and culturally acceptable within medical training environments.

CONCLUSION

This case-control study provides evidence that excessive smartphone-based academic engagement constitutes a distinct and independently significant risk factor for treatment-resistant anxiety among medical students, with students in the highest exposure quartile carrying a more than four-fold adjusted odds of treatment resistance (AOR = 4.58; 95% CI: 2.33–9.01) and those using smartphones for academic purposes for more than six hours daily facing a 3.72-fold elevated risk (95% CI: 1.91–7.23) compared with lower-exposure peers, after adjustment for sleep duration, academic workload, age, and gender; the dose-response gradient across SBLEI tertiles, in which treatment-resistant prevalence escalated from 6.7% in the low-exposure band to 96.7% in the highest band, further implicates a clinically meaningful exposure threshold at an SBLEI score of approximately 40, above which the risk of therapy-refractory anxiety becomes near-universal. These findings, taken together with the strong independent contribution of sleep curtailment below six hours per night (AOR = 2.84), indicate that effective prevention and management of severe anxiety in digitally immersed medical students will require not only conventional psychotherapeutic and pharmacological strategies but the integration of structured screen-time guidelines, specifically, limiting continuous academic smartphone use to periods not exceeding two hours without a scheduled break and capping total daily academic screen exposure at a maximum of five to six hours, alongside mandatory sleep hygiene education and institutional mental health support embedded within medical curricula to safeguard the psychological wellbeing of future healthcare professionals in an increasingly technology-dependent educational landscape.

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