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ORIGINAL ARTICLE

Observational Study on the Relationship Between Chronic Stress and the Development of Autoimmune Diseases

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ABSTRACT:

Background: Autoimmune diseases arise from dysregulated immune responses and are influenced by a combination of genetic, environmental, hormonal, and psychosocial factors. Among these, chronic psychological stress has increasingly been recognized as a significant contributor to immune imbalance, heightened inflammation, and disease exacerbation. Understanding the relationship between chronic stress and autoimmune disease activity is essential for developing comprehensive management strategies that address both physiological and psychosocial dimensions of patient care. **Aim:** To assess the relationship between chronic stress and the development and severity of autoimmune diseases among patients attending a tertiary care hospital, using psychological stress assessment tools, biological stress markers, and lifestyle factors. **Materials and Methods:** This observational study included 72 patients diagnosed with various autoimmune diseases. Chronic stress levels were evaluated using validated instruments, including the Perceived Stress Scale (PSS-10) and the Hospital Anxiety and Depression Scale (HADS). Biological indicators of stress such as morning salivary cortisol, heart rate variability (HRV), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were recorded. Autoimmune disease activity was assessed through standardized scoring systems and relevant laboratory investigations. Lifestyle factors including sleep duration, physical activity, smoking, and alcohol use were also analyzed for their association with stress. **Results:** Moderate and high stress levels were observed in 47.22% and 36.11% of patients, respectively, and were strongly associated with increased autoimmune disease severity ($p < 0.001$). Elevated cortisol levels were present in 38.89% of patients and correlated with a higher mean disease activity score (7.2 ± 2.4). Low HRV was identified in 43.06% of the cohort and was significantly associated with greater disease activity ($p = 0.002$). Inflammatory markers were elevated in more than half of the participants, with CRP elevated in 55.56% and ESR in 61.11%. Lifestyle factors such as inadequate sleep ($p = 0.021$) and sedentary behavior ($p = 0.014$) demonstrated significant associations with higher stress levels. **Conclusion:** Chronic stress significantly influences the severity and activity of autoimmune diseases, with strong associations observed across psychological, biological, and lifestyle domains. These findings highlight the need for integrated stress-management approaches alongside conventional medical treatment to improve patient outcomes.

Keywords: Chronic Stress, Autoimmune Diseases, Cortisol, Inflammation, Disease Severity

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INTRODUCTION

Autoimmune diseases represent a diverse group of chronic conditions characterized by dysregulated immune responses in which the body's defense system mistakenly targets its own tissues. These disorders, which include rheumatoid arthritis, systemic lupus erythematosus, autoimmune thyroiditis, inflammatory bowel disease, psoriasis, and multiple sclerosis, affect millions of individuals worldwide and are associated with substantial morbidity, disability, and healthcare burden. Although the exact etiologies of autoimmune diseases remain incompletely understood, substantial evidence suggests that their development is multifactorial, involving complex interactions among genetic susceptibility, hormonal influences, environmental exposures, infections, and psychosocial factors. In recent years, chronic psychological stress has gained increasing attention as a potentially significant, yet often underrecognized, contributor to autoimmune disease onset and progression.[1]Chronic stress is broadly conceptualized as a prolonged state of psychological and physiological tension that develops when an individual perceives that environmental demands exceed their adaptive capacity. Unlike acute stress—which can trigger short-term adaptive responses—chronic stress exerts sustained effects on neuroendocrine pathways, inflammatory processes, autonomic function, and cellular immunity. Persistent activation of the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system results in hormonal imbalances, altered cortisol secretion, dysregulated catecholamine production, and impaired negative feedback mechanisms. Over time, these changes promote immune dysregulation, including enhancement of pro-inflammatory cytokine release, reduced immunologic tolerance, and shifts in T-cell balance. Such pathways have been implicated in the initiation and exacerbation of autoimmune activity, suggesting that chronic stress may contribute not only to symptom flares but also to disease susceptibility itself.[2] The relationship between chronic stress and immune function has been well-established across multiple experimental studies. Research has

demonstrated that stress can modulate both innate and adaptive immunity by influencing immune cell trafficking, antibody production, cytokine profiles, and inflammatory signaling pathways. Stress-related hormones such as cortisol and adrenaline, though adaptive during short-term challenges, can become maladaptive when continuously elevated, leading to immune suppression in some contexts while promoting inappropriate immune activation in others. These opposing effects underscore the complexity of stress biology and its capacity to shape autoimmune processes in genetically predisposed individuals. Furthermore, psychological stress has been linked with increased production of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other key inflammatory mediators known to drive autoimmunity.[3] In addition to biological mechanisms, behavioral pathways provide another link between stress and autoimmune disorders. Individuals experiencing chronic stress are more likely to engage in unhealthy lifestyle behaviors such as inadequate sleep, sedentariness, poor diet, smoking, and alcohol consumption. These behaviors themselves can exacerbate immune dysfunction and inflammation, creating a complex network of interactions between lifestyle, stress, and immunological health. Sleep disturbances, for example, have been associated with increased inflammatory marker levels and heightened immune reactivity, while physical inactivity has been linked with impaired metabolic function and chronic low-grade inflammation. Thus, lifestyle factors may mediate or amplify the effects of stress on autoimmune disease outcomes.[4,5] Although many studies have explored the immunological consequences of stress in healthy individuals, fewer have examined its specific association with autoimmune disease development or severity. Existing research suggests that individuals with autoimmune disorders often report higher stress levels compared to healthy controls and that stress frequently precipitates disease flares or worsening of symptoms. Evidence also indicates that stressful life events—such as bereavement, job strain, interpersonal conflict, or chronic caregiving—may precede the onset of autoimmune diseases in some patients. Nevertheless, the relationship between stress exposure and measurable disease activity in clinical populations remains insufficiently characterized, particularly in diverse healthcare settings.

MATERIALS AND METHODS

This observational study was conducted to evaluate the relationship between chronic stress and the development of autoimmune diseases among patients attending a tertiary care hospital. The study followed a structured clinical observation framework in which eligible participants were assessed for indicators of chronic psychological stress and screened for clinical, biochemical, and immunological features associated with autoimmune disorders. No interventions were introduced at any stage; all assessments were based on routine clinical evaluations, validated questionnaires, and laboratory investigations.

The study was carried out in a tertiary care hospital that receives referrals from both urban and rural regions, ensuring a diverse patient population. A total of 72 patients were included based on predefined inclusion and exclusion criteria. All participants were recruited from outpatient and inpatient departments specializing in internal medicine, rheumatology, endocrinology, and psychiatry. Patients were approached consecutively, and those meeting the criteria were invited to participate after providing informed consent.

Inclusion Criteria

Participants were eligible for inclusion if they were adults aged 18 years or above with a confirmed diagnosis or clinical suspicion of autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, psoriasis, or inflammatory bowel disease. Patients were required to have the ability to understand and respond to stress assessment tools, and willingness to provide relevant medical, lifestyle, and psychosocial information. Both newly diagnosed and previously diagnosed cases were included to capture a broad range of autoimmune activity and stress exposure patterns.

Exclusion Criteria

Patients were excluded if they had acute infections, malignancies, severe psychiatric illnesses interfering with evaluation, or were on long-term corticosteroids or immunosuppressive therapy initiated for non-autoimmune reasons. Those with cognitive impairments, substance abuse disorders, or incomplete medical records were also excluded to maintain data quality and avoid confounding influences that might distort the stress–autoimmunity relationship.

Assessment of Chronic Stress

Chronic stress levels were evaluated using validated psychological instruments, including the Perceived Stress Scale (PSS-10), Hospital Anxiety and Depression Scale (HADS), and a structured stressor checklist tailored to socioeconomic, occupational, and familial domains. In addition to psychometric scores, biological markers of stress were documented, including morning salivary cortisol levels, heart rate variability (HRV) measurements, sleep quality indices, and autonomic symptoms. Stress-related lifestyle behaviors such as sleep duration, physical inactivity, smoking, alcohol consumption, and dietary irregularities were assessed through structured interviews.

Assessment of Autoimmune Disease Activity

Autoimmune disease activity was evaluated using standardized clinical scoring systems relevant to each

condition, such as DAS28 for rheumatoid arthritis, SLEDAI for systemic lupus erythematosus, and thyroid function scoring for autoimmune thyroid disorders. Physical examinations were performed to assess joint tenderness, swelling, skin lesions, mucosal involvement, neurological deficits, or gastrointestinal symptoms. Laboratory parameters including complete blood counts, ESR, CRP, ANA, anti-dsDNA, rheumatoid factor, anti-CCP, thyroid antibodies, complement levels (C3, C4), and other disease-specific biomarkers were recorded when applicable. Imaging studies such as ultrasonography and MRI were reviewed for relevant structural or inflammatory changes whenever available.

Data Collection Procedures

All data were collected using a structured proforma that included demographic information, detailed medical history, family history of autoimmune conditions, psychosocial stressors, environmental exposures, sleep history, and work-related characteristics. Clinical evaluations were performed by trained physicians, and psychometric assessments were administered by psychology-trained personnel to ensure consistency. Laboratory results were obtained from the hospital's central diagnostic facility to maintain uniformity in testing methodology. All patient information was anonymized, coded, and stored securely.

Outcome Measures

Primary outcome measures included the association between chronic stress levels and autoimmune disease presence or severity. Secondary outcomes included correlations between stress biomarkers and autoimmune activity scores, the influence of lifestyle-related stress factors on disease characteristics, and identification of high-risk stress profiles contributing to autoimmune manifestations. Patterns of symptom exacerbation during high-stress periods and stress-related flare-ups were also examined through patient self-reports and clinical records.

RESULTS

Table 1: Demographic Characteristics of the Study Population

The demographic profile of the 72 patients revealed that the majority of participants were within the middle-aged groups. The highest proportion belonged to the 31–45-year age category, representing 36.11% of the cohort, followed closely by individuals aged 46–60 years (33.33%). Younger adults aged 18–30 years constituted 13.89%, whereas the elderly group above 60 years comprised 16.67%. This distribution suggests that autoimmune diseases were more prevalent in middle-aged individuals. Female patients accounted for a significantly larger portion of the sample (69.44%) compared to males (30.56%), aligning with existing literature showing higher autoimmune disease predisposition among females. Regarding residence, 56.94% of the participants were from urban areas, while 43.06% resided in rural settings. This may reflect increased healthcare-seeking behavior, accessibility to tertiary care, or higher stress exposure in urban populations.

Table 2: Distribution of Autoimmune Diseases Among Patients

The analysis of autoimmune conditions demonstrated that rheumatoid arthritis (RA) was the most common disease among the study participants, affecting 36.11% of the sample. Hashimoto's thyroiditis was the second most prevalent (25.00%), indicating a significant burden of autoimmune endocrine disorders. Systemic lupus erythematosus (SLE) accounted for 16.67% of cases, which is consistent with its known predominance among women of reproductive age. Psoriasis constituted 8.33% of the participants, showing a moderate representation of autoimmune dermatological disorders. Both inflammatory bowel disease (IBD) and multiple sclerosis (MS) were the least frequent, each accounting for 6.94% of the sample. These findings reflect a varied distribution of autoimmune diseases, with rheumatologic and thyroid-related disorders being most prominent.

Table 3: Chronic Stress Levels and Autoimmune Disease Severity

Assessment of chronic stress using the PSS-10 scale revealed that the majority of patients (47.22%) experienced moderate stress, followed by 36.11% who exhibited high stress levels. Only 16.67% reported low stress. A strong association was observed between chronic stress and autoimmune disease severity. Patients with low stress demonstrated a mean severity score of 3.8 ± 1.2, whereas those with moderate stress had a higher mean score of 5.6 ± 1.9, with a statistically significant p-value of 0.003. The most clinically significant finding was among patients with high stress levels, who displayed the highest mean severity score of 7.4 ± 2.1. This association was highly significant ($p < 0.001$), indicating that disease severity increased proportionately with stress levels. These results emphasize that chronic stress plays a substantial role in influencing disease activity and symptom burden among individuals with autoimmune disorders.

Table 4: Stress Biomarkers and Autoimmune Disease Activity

The evaluation of biological stress markers further supported the relationship between stress and autoimmune disease activity. Elevated morning salivary cortisol levels were observed in 38.89% of patients, and these individuals exhibited a higher mean disease activity score of 7.2 ± 2.4, with a significant p-value of 0.001. Low heart rate variability (HRV), a physiological indicator of chronic stress, was detected in 43.06% of participants, who also had

a significantly increased mean activity score of 6.9 ± 2.0 (p = 0.002). Markers of systemic inflammation were notably elevated, with 55.56% of patients presenting raised C-reactive protein (CRP) levels and 61.11% demonstrating elevated erythrocyte sedimentation rate (ESR). Patients with abnormal CRP values had the highest mean activity score at 7.7 ± 2.5, with a highly significant p-value (<0.001), while elevated ESR levels were also associated with significantly greater disease activity (p = 0.004). These findings indicate strong correlations between physiological stress markers and autoimmune disease severity, suggesting that chronic stress exacerbates inflammatory processes.

Table 5: Lifestyle Factors Associated with Chronic Stress

Lifestyle assessment revealed several behavioral factors associated with chronic stress. Short sleep duration (<6 hours) was observed in 40.28% of participants, while nearly half (45.83%) slept 6–8 hours. A statistically significant association was found between adequate sleep (6–8 hours) and lower stress levels (p = 0.021), indicating sleep as an important protective factor. More than half of the patients (52.78%) reported a sedentary lifestyle, which showed a strong association with elevated stress levels (p = 0.014), highlighting physical inactivity as a key contributor to chronic stress. Smoking and alcohol consumption were reported by 23.61% and 26.39% of participants, respectively, but their associations with stress levels were not statistically significant (p = 0.089 and p = 0.074). These results suggest that although substance use may influence stress, sleep and physical activity patterns play more substantial and statistically meaningful roles in modulating chronic stress among individuals with autoimmune diseases.

Table 1: Demographic Characteristics of the Study Population (N = 72)

Variable	Category	Frequency (n)	Percentage (%)
Age Group (years)	18–30	10	13.89%
	31–45	26	36.11%
	46–60	24	33.33%
	>60	12	16.67%
Gender	Male	22	30.56%
	Female	50	69.44%
Residence	Urban	41	56.94%
	Rural	31	43.06%

Table 2: Distribution of Autoimmune Diseases among Patients (N = 72)

Autoimmune Condition	Frequency (n)	Percentage (%)
Rheumatoid Arthritis (RA)	26	36.11%
Systemic Lupus Erythematosus (SLE)	12	16.67%
Hashimoto's Thyroiditis	18	25.00%
Psoriasis	6	8.33%
Inflammatory Bowel Disease (IBD)	5	6.94%
Multiple Sclerosis (MS)	5	6.94%

Table 3: Distribution of Chronic Stress Levels (Based on PSS-10) and Autoimmune Disease Severity

Stress Level	Frequency (n)	Percentage (%)	Mean Disease Severity Score (±SD)	p-value*
Low Stress	12	16.67%	3.8 ± 1.2	
Moderate Stress	34	47.22%	5.6 ± 1.9	**0.003**
High Stress	26	36.11%	7.4 ± 2.1	**<0.001**

*p-value using ANOVA comparing autoimmune disease severity across stress levels.

Table 4: Association Between Stress Biomarkers and Autoimmune Disease Activity (N = 72)

Biomarker	Normal Range	Abnormal (n)	Abnormal (%)	Mean Activity Score (±SD)	p-value*
Morning Salivary Cortisol (elevated)	<19 µg/dL	28	38.89%	7.2 ± 2.4	**0.001**
HRV (Low)	<50 ms	31	43.06%	6.9 ± 2.0	**0.002**
CRP (Elevated)	>6 mg/L	40	55.56%	7.7 ± 2.5	**<0.001**
ESR (Elevated)	>20 mm/hr	44	61.11%	7.4 ± 2.3	**0.004**

*p-value using independent t-test comparing normal vs abnormal biomarker levels.

Table 5: Lifestyle Factors Associated with Chronic Stress (N = 72)

Lifestyle Parameter	Category	Frequency (n)	Percentage (%)	p-value*
Sleep Duration	<6 hours	29	40.28%	
	6–8 hours	33	45.83%	**0.021**
	>8 hours	10	13.89%	
Physical Activity	Sedentary	38	52.78%	**0.014**
	Moderate/Active	34	47.22%	
Smoking	Yes	17	23.61%	0.089
Alcohol Use	Yes	19	26.39%	0.074

*p-value showing association of each factor with high chronic stress levels (Chi-square test).

DISCUSSION

In our study, the female predominance (69.44%) among patients aligns with the established observation that autoimmune diseases occur more frequently in women. For example, a multilevel review by Roald et al. (2003) noted that women are approximately two-to-three times more likely to develop rheumatoid arthritis (RA) and related autoimmune conditions compared to men,[6] suggesting that the gender skew in our cohort is consistent with broader epidemiologic patterns. The fact that 36.11% of our subjects were aged 31-45 years and 33.33% aged 46-60 years further supports the typical age range for onset of autoimmune disorders in adults.

The distribution of disease types in our study—RA (36.11%), Hashimoto's thyroiditis (25.00%), SLE (16.67%)—is broadly consistent with prior work showing RA as the most common autoimmune diagnosis in many rheumatology settings. For instance, Henriksson et al. (2002) observed RA prevalence as the dominant autoimmune disorder in their clinic-based series,[7] providing a useful comparator to our 36.11% figure. Our relatively higher prevalence of thyroid autoimmune disease (25.00%) also echoes findings from epidemiologic studies that show endocrine autoimmunity as a significant comorbidity in multi-disease autoimmune cohorts.

Regarding the link between chronic stress levels and disease severity, our data show that patients with high stress (36.11%) had a mean severity score of 7.4 ± 2.1, significantly higher than moderate stress (5.6 ± 1.9) or low stress (3.8 ± 1.2). This echoes the results of Evers et al. (2012), who found that in RA patients (n=80) daily stressors and worry predicted increased disease activity one month later (though they did not give the exact mean scores we used).[8] Our quantitative stratification adds concrete values to this relationship, reinforcing that higher perceived stress correlates with higher autoimmune disease severity.

In examining stress biomarkers, we found elevated salivary cortisol in 38.89% of patients (mean activity score 7.2 ± 2.4), low HRV in 43.06% (6.9 ± 2.0), elevated CRP in 55.56% (7.7 ± 2.5) and elevated ESR in 61.11% (7.4 ± 2.3). Earlier mechanistic work by Chikanza et al. (1992) demonstrated HPA-axis dysregulation and elevated cortisol in RA patients compared to controls,[9] which supports our finding of cortisol elevation in ~39% of patients. Our study further bridges that physiological deficiency to disease activity scores.

Lifestyle factors in our cohort also showed significant associations: 40.28% had sleep duration <6 hrs, 45.83% slept 6-8 hrs (and this group had lower stress with p=0.021), and 52.78% were sedentary (p=0.014). A classic sleep-autoimmunity linkage was shown by Irwin et al. (1996), who demonstrated that sleep deprivation increased inflammatory markers in healthy adults,[10] suggesting a plausible pathway for our finding that inadequate sleep aligns with elevated stress and likely higher disease burden.

Our urban vs rural residence breakdown (56.94% urban, 43.06% rural) suggests potentially higher stress exposure or better tertiary-care access in urban areas. Although older literature did not always stratify by residence, the work of Vant Hof et al. (2005) found that urban living correlated with higher autoimmune disease incidence, possibly due to environmental and psychosocial stressors.[11] Our findings are compatible with that pattern.

Finally, the incremental increase in disease severity across stress strata (3.8 → 5.6 → 7.4) highlights a dose-response type relationship that is seldom quantified in older literature. The review by Black & Goldstein (2007) summarised the stress-immune dysregulation model in autoimmunity but lacked numeric severity gradients,[12] so our data help fill that gap.

CONCLUSION

The present study demonstrates a clear association between chronic stress and increased severity of autoimmune diseases, as evidenced by both psychological assessments and biological stress markers. Higher stress levels were consistently linked with elevated disease activity scores and heightened inflammatory responses. Lifestyle factors such as inadequate sleep and sedentary behaviour further amplified stress and its impact on autoimmune conditions. These findings highlight the importance of integrating stress-management strategies into routine care to improve outcomes for patients with autoimmune diseases.

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