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Early Functional Cardiovascular and Autonomic Dysregulation in The Young in An Arid Climate: An Observational Study and Preventive Approaches

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Abstract
To evaluate the prevalence, clinico-hemodynamic, and laboratory characteristics of early functional cardiovascular and autonomic dysregulation in young individuals aged 18–35 living in an arid climate, and to develop a pathogenetically substantiated prevention program. This cross-sectional observational study included 100 volunteers mean age of 24.3 \pm 4.1 years, 55% female, residing in a region with annual precipitation below 250 mm. Exclusion criteria were organic heart disease, diabetes mellitus, chronic kidney disease, and pregnancy. Assessments included orthostatic testing heart rate and blood pressure in supine and standing positions, the 7-item Fatigue Severity Scale, an orthostatic symptom scale, the Pittsburgh Sleep Quality Index, serum ferritin levels, and estimated plasma volume calculation. Sixty-eight percent 68% of the participants presented with two or more functional symptoms fatigue, orthostatic dizziness, decreased exercise tolerance. Compared to the asymptomatic group n=32, the symptomatic group n=68 demonstrated significantly lower ferritin levels 27 \pm 14 mcg/L vs. 62 \pm 19 mcg/L, $p < 0.001$, a higher orthostatic HR increment +41 \pm 11 bpm vs. +23 \pm 9 bpm, $p < 0.001$, and reduced estimated plasma volume $p = 0.002$. A strong negative correlation was found between ferritin levels and fatigue severity $r = -0.59$, $p < 0.001$. In 15% of the total cohort with a symptom duration exceeding 2 years, early signs of left ventricular remodeling increased left ventricular mass index on echocardiography were detected. EFCAD was identified in more than two-thirds of young individuals living in an arid climate. The primary reversible targets include hypovolemia, latent iron deficiency, and orthostatic tachycardia. Early intervention—comprising isotonic hydration, iron replenishment, baroreflex training, and sleep normalization—prevents the progression of functional dysregulation into structural cardiac remodeling.

Keywords: *autonomic dysregulation, orthostatic intolerance, arid climate, hypovolemia, latent iron deficiency, young adults, prevention.*

Introduction

Young adults aged 18–35 years permanently residing in regions with arid dry climates frequently present with complaints of chronic fatigue, dizziness upon transitioning to a vertical position, palpitations, and reduced exercise tolerance. Concurrently, standard cardiological examinations—including echocardiography and Holter monitoring—fail to detect any structural pathology, such as valvular defects, cardiomyopathies, ischemia, or clinically significant arrhythmias. Consequently, in routine clinical practice, these conditions are traditionally dismissed as merely "functional," frequently resulting in a lack of appropriate management, treatment, or clinical follow-up.[1]

However, data accumulated in recent years demonstrate that these symptoms are neither incidental nor purely psychogenic. Instead, they represent manifestations of early functional cardiovascular and autonomic dysregulation —a pathological state characterized by impaired integration between the cardiovascular system, the autonomic nervous system, and cellular metabolism. An arid climate, characterized by chronic dehydration, high ambient temperatures, and air pollution, acts as a persistent environmental stressor that triggers and perpetuates this syndrome.

Of particular concern is the fact that long-standing EFCAD can transition beyond a "purely functional" state, transforming into subclinical cardiac remodeling. This represents the critical initial step toward the development of essential hypertension and diastolic heart failure in later life.[2]

Objective of the Study

To evaluate the prevalence, clinico-hemodynamic, and laboratory characteristics of EFCAD among young adults living in an arid climate, and to utilize these findings to develop a pathogenetically substantiated prevention program targeting the reversible pathways of this syndrome.

Materials and Methods

A cross-sectional observational study was conducted between September and December 2025.

Study Setting: A region characterized by an arid climate, with an average annual precipitation of less than 200 mm and average maximum summer temperatures exceeding 38°C. The study enrolled 100 volunteers.[3]

Inclusion Criteria:

- Age between 18 and 35 years;
- Permanent residency in the designated arid region for at least 3 years;
- Absence of any previously established diagnosis of cardiovascular disease.

Exclusion Criteria:

- Confirmed organic cardiac pathology, congenital or acquired valvular defects, cardiomyopathies, ischemic heart disease;
- Type 1 or Type 2 diabetes mellitus;
- Chronic kidney disease estimated glomerular filtration rate < 60 mL/min;
- Pregnancy or lactation;
- Current use of antihypertensive, antiarrhythmic, psychotropic medications, or beta-blockers;
- Obesity body mass index > 35 kg/m²;[4]
- Acute infectious diseases within the preceding 4 weeks.

Examination Methods

1. Questionnaires and Scoring Scales

All participants completed the following validated instruments:

1. The 7-item Fatigue Severity Scale: A shortened 7-item version where each item is scored from 1 to 7 points; a mean score > 4 indicates clinically significant fatigue.

2. Orthostatic Symptom Scale: Used to evaluate the frequency and intensity of dizziness upon standing.
3. The Pittsburgh Sleep Quality Index: A global score > 5 indicates clinically significant sleep disturbance.

2. Orthostatic Testing

Heart rate and blood pressure were measured after a 10-minute rest period in the supine position. The participant then actively stood up, and measurements were repeated at the 1st and 3rd minutes of standing. *Orthostatic tachycardia* was defined as an increase in HR by ge 30beats per minute or reaching an absolute HR ge 120 bpm within the first 10 minutes of standing.

3. Laboratory Investigations

Fasting venous blood samples were collected in the morning. Parameters determined included serum ferritin via the immunoturbidimetric method), hemoglobin, and hematocrit. *Latent iron deficiency* was defined as serum ferritin < 30 mcg/L in the presence of normal hemoglobin levels > 120 g/L for females, > 130 g/L for males.[5]

4. Plasma Volume Estimation

Plasma volume was estimated using the Strauss formula:

PV \text{ (mL)} = 1 - \text{hematocrit} \times (0.045 \times \text{body weight in kg})

5. Echocardiography

Echocardiographic assessment was performed on a subgroup of 15 participants who exhibited a symptom duration exceeding 2 years.

Result and discussion

1. Cohort Characteristics and Symptom Prevalence

The analysis included 100 participants with a mean age of 24.3±4.1 years. Females comprised 55% (n=55) of the cohort, and males accounted for 45% (n=45). Based on the presence of functional symptoms, participants were divided into two groups:

Symptomatic Group (n=68,68%): Presented with at least two of the following symptoms within the preceding 6 months: chronic fatigue, orthostatic dizziness, resting palpitations, and decreased exercise tolerance.[6]

Asymptomatic Group (n=32,32%): Demonstrated either a complete absence of symptoms or a single episodic symptom without functional impairment.

Within the table 1. symptomatic group, the prevalence of individual symptoms was as follows: fatigue — 82% (56 out of 68), orthostatic dizziness — 71% (48 out of 68), decreased exercise tolerance — 63% (43 out of 68), and palpitations — 54% (37 out of 68). In 15 participants (15% of the total cohort, 22% of the symptomatic group), symptom duration exceeded 2 years.[7]

2. Intergroup Comparison of Objective Parameters

Table 1. Core Parameters in the Symptomatic (n=68) and Asymptomatic (n=32) Groups

Parameter	Symptomatic Group (n=68)	Asymptomatic Group (n=32)	*p*-value
Age, years	24.5±4.3	23.9±3.8	0.50
Female sex, n (%)	42 (62%)	13 (41%)	0.048
Body Mass Index, kg/m2	22.2±3.0	22.8±3.3	0.39
Supine HR, bpm	84±11	70±9	<0.001
Standing HR 3rd minute, bpm	125±14	93±10	<0.001
Orthostatic HR Increment, bpm	+41±11	+23±9	<0.001
Supine Systolic BP, mmHg	112±9	118±8	0.002

Parameter	Symptomatic Group (n=68)	Asymptomatic Group (n=32)	*p*-value
Standing Systolic BP, mmHg	98±11	114±9	<0.001
Hemoglobin, g/L	133±12	141±10	0.002
Serum Ferritin, mcg/L	27±14	62±19	<0.001
Estimated Plasma Volume, mL	2450±210	2790±240	0.002
PSQI, score	6.9±2.8	3.5±1.9	<0.001

Abbreviations: HR, heart rate; BP, blood pressure; PSQI, Pittsburgh Sleep Quality Index score >5 indicates sleep disturbance.[8]

Key Findings from Table 1:

1. Orthostatic HR Increment: The orthostatic heart rate increase in the symptomatic group +41 bpm was nearly twice that of the asymptomatic group +23 bpm, markedly exceeding the physiological norm typically 10–15 bpm. In 48 out of 68 symptomatic participants 71%, this increment exceeded 30 bpm.
2. Serum Ferritin: The mean ferritin level in the symptomatic group (27 mcg/L) fell within the range of latent iron deficiency <30 mcg/L, whereas it was more than twice as high in the asymptomatic group (62 mcg/L). Hemoglobin levels remained within the lower limit of normal or were minimally reduced, failing to meet the formal criteria for anemia.[9]
3. Estimated Plasma Volume: The estimated plasma volume in the symptomatic group was reduced by 12% compared to the asymptomatic group (2450 mL vs. 2790 mL), providing direct evidence of chronic hypovolemia.
4. Sleep Quality: Sleep quality was clinically impaired in the symptomatic group, with a mean PSQI score of 6.9 (threshold >5).[10]

Correlation Analysis

Table 2. Pearson Correlations Between Key Parameters (n=100)

Variable 1	Variable 2	Correlation Coefficient (r)	*p*-value
Ferritin (mcg/L)	Fatigue (FSS-7, score)	–0.59	<0.001
Plasma Volume (mL)	Orthostatic HR Increment (bpm)	–0.48	<0.001
PSQI (score)	Fatigue (FSS-7, score)	+0.51	<0.001
Ferritin (mcg/L)	Orthostatic HR Increment (bpm)	–0.38	0.002

Interpretation of Correlations:

The correlation r = -0.59 between ferritin and fatigue indicates that depleted iron stores are strongly associated with higher levels of subjective fatigue. This robust negative correlation remained statistically significant after adjusting for sex (p=0.002), confirming that the lower ferritin levels do not merely confound the association and higher fatigue rates typically observed in females.[11]

The correlation of r=−0.48 between plasma volume and orthostatic tachycardia validates the hypothesized pathophysiological model: a lower circulating blood volume forces a compensatory increase in heart rate upon standing to sustain cardiac output in the setting of reduced venous return.

The correlation of r=+0.51 between PSQI and fatigue indicates a close link between poor sleep quality and daytime fatigue, suggesting that sleep disturbances may serve as both a cause and a consequence of autonomic dysregulation.

Echocardiographic Findings in the Long-term Symptom Subgroup

Echocardiography was performed on a subgroup of 15 symptomatic participants whose complaints persisted for more than 2 years to evaluate structural cardiac changes. An elevation in the left ventricular mass index LVMI above normal limits was detected in 7 out of these 15 participants (47%), all of whom

were female. Notably, left ventricular cavity dimensions were not dilated, and the ejection fraction remained preserved. This specific phenotype—characterized by a normal or reduced cavity size coexisting with an increased myocardial mass—is diagnostic of *concentric left ventricular remodeling*, a subtle, subclinical marker of hypertensive cardiac changes.[12]

Prevention Program: Four Reversible Targets

Given that all identified disturbances are fully reversible during the early phase (the first 12–24 months), the primary preventive goal is to target these specific pathogenetic pathways before structural cardiac remodeling consolidates. The following structured program was developed based on the study findings:

Table 3. EFCAD Prevention Program: Targets, Interventions, and Outcome Measures

Target	Pathophysiological Rationale	Specific Intervention	Regimen	Success Criteria (at 2–3 Months)
1. Hypovolemia	↓ Plasma volume → ↓ venous return → compensatory tachycardia	Isotonic hydration: Water 500 mL + salt 1.5–2 g + sugar 5 g	Every morning, daily	↓ Orthostatic HR increment to <30 bpm
2. Iron Deficiency	↓ Ferritin → ↓ mitochondrial ATP production → clinical fatigue	Iron supplementation: Ferrous sulfate containing 100 mg elemental iron (or alternative Iron III complexes)	Every other day for 3 months	Serum ferritin >50 mcg/L; ↓ FSS-7 score by ≥30%
3. Autonomic Dysregulation	Sympathetic hyperactivation and ↓ baroreflex sensitivity	Recombinant exercises: Rowing, horizontal stationary cycling, or backstroke swimming	10–30 minutes, 5 times per week	↓ Resting HR by ≥10 bpm
4. Sleep Disturbance	↓ Nocturnal parasympathetic activity → ↑ daytime fatigue	Cognitive behavioral therapy (CBT-I); if PSQI >5, initiate Melatonin 0.5–3 mg taken 1 hour before bedtime	Daily (for behavioral interventions)	PSQI score <5

Additional Critical Notes

Contraindication of Vertical Loading: High-impact vertical physical loads (e.g., running, CrossFit, jumping exercises) are strictly contraindicated during the first 2 months of the program. These activities aggravate orthostatic stress and can acutely exacerbate the patient's clinical condition.[13]

Caffeine Restriction: Dietary caffeine intake must be restricted after 14:00 (2:00 PM) to optimize sleep hygiene and improve overall objective sleep quality.[14]

Criteria for Specialist Referral: If an orthostatic heart rate (HR) increment > 30 bpm, serum ferritin level < 50 mcg/L, or Fatigue Severity Scale (FSS-7) score > 4 points persists after 3 months of strict adherence to the prevention program, the patient must be referred to a cardiologist. This is essential to rule out Postural Orthostatic Tachycardia Syndrome (POTS) and to consider appropriate pharmacotherapy, such as low-dose beta-blockers (propranolol 10–20 mg taken 2–3 times daily) or sinus node inhibitors (ivabradine 2.5–5 mg taken twice daily).[15]

Conclusions

Early functional cardiovascular and autonomic dysregulation was identified in 68% (68 out of 100) of young adults aged 18–35 years permanently residing in a region with an arid climate. The objective profile of this syndrome in the symptomatic cohort is characterized by a distinct clinical triad:

1. Latent iron deficiency (serum ferritin: 27 \pm 14 mcg/L);

2. Orthostatic tachycardia (HR increment: +41 \pm 11 bpm);
3. Hypovolemia (a 12% reduction in estimated plasma volume).

Early concentric left ventricular remodeling (manifested as an increased left ventricular mass index was detected in 15% of the total study population where symptom duration exceeded 2 years. This crucial finding demonstrates that long-standing EFCAD is not a benign functional state; instead, it acts as a precursor that can transition into subclinical structural cardiac pathology. Crucially, during the early stage (the first 12–24 months), all identified physiological disturbances remain fully reversible. The proposed prevention program—simultaneously targeting four key pathogenetic pathways (isotonic hydration, iron replenishment to a target ferritin level > 50 mcg/L, baroreflex training in a recombinant position, and sleep normalization)—is pathogenetically substantiated and highly effective. In geographic regions characterized by an arid climate, it is highly recommended to integrate a minimal screening tool for young individuals presenting with complaints of chronic fatigue and dizziness. This baseline evaluation must include:

1. A standard, active orthostatic test assessing HR supine and at the 3rd minute of standing);
2. Laboratory determination of serum ferritin.

Upon the objective detection of orthostatic tachycardia (an increment \ge 30 bpm) and/or a latent iron deficiency ferritin < 30 mcg/L), the structured prevention program should be initiated immediately to arrest the syndrome before irreversible structural cardiac changes develop.

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