

Long-term Cardiovascular Recovery Patterns in Women Post-COVID-19. A Multi-center Prospective Analysis from Middle Eastern Cohorts

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Abstract

Background: Long COVID syndrome affects approximately 10-30% of survivors, with women demonstrating consistently higher rates of persistent cardiac symptoms. Yet longitudinal data on cardiovascular recovery trajectories in female patients from the Middle East remain notably sparse.

Objectives: To characterize cardiac function recovery patterns in women at 12 and 24 months following COVID-19 infection, utilizing cardiovascular magnetic resonance (CMR) imaging and established biomarker panels.

Methods: We conducted a prospective cohort study encompassing 4,892 women (mean age 42.3±8.7 years) across 12 academic and tertiary centers in six Gulf Cooperation Council states. Participants underwent CMR and biomarker assessment (troponin I, NT-proBNP, CRP) at 3, 12, and 24 months post-infection. Mixed-effects models and survival analysis were employed to identify predictors of delayed recovery.

Results: Persistent myocarditis was evident in 1,895 participants (38.7%) at 12 months, decreasing modestly to 34.2% by 24 months ($p < 0.001$ for trend). NT-proBNP levels remained 45% higher in symptomatic versus recovered women (median 168 vs 116 pg/mL, $p < 0.001$). Hospitalization during acute infection (OR=1.89, 95% CI: 1.52-2.34) and metabolic syndrome (OR=2.11, 95% CI: 1.78-2.49) emerged as the most significant predictors of impaired recovery.

Conclusions: This study demonstrates that women in the Middle East experience protracted and heterogeneous cardiac recovery following COVID-19. Our findings advocate for extended 24-month surveillance protocols tailored to regional risk profiles.

Keywords: Post-COVID-19 syndrome, cardiovascular sequelae, cardiac MRI, Middle East cohort, female-specific outcomes.



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Introduction

Since the pandemic's emergence in late 2019, SARS-CoV-2 has infected over 700 million individuals globally [1]. While most patients achieve full recovery, a substantial subset—estimated

between 10-30%—develop persistent symptoms collectively termed Long COVID [2]. Growing evidence suggests women face a 1.5-2 fold higher risk of developing this syndrome, particularly cardiovascular and neurological manifestations [3].

Sex-based biological differences appear central to this disparity. Estrogen-mediated upregulation of ACE2 receptor expression, the virus's primary entry point, may trigger distinct immune responses in women [4]. Moreover, acute COVID-19 precipitates myocarditis in 20-30% of severe cases, yet data on chronic myocardial inflammation remain fragmentary [5].

The Middle Eastern context renders this question particularly urgent. Recent epidemiological surveys indicate that obesity and metabolic syndrome prevalence among Gulf women exceeds global averages by 35-40% [6]. Compounding this, the vast majority of large-scale Long COVID research has concentrated on European and North American populations, leaving Middle Eastern cohorts severely underrepresented [7]. A recent Saudi study of 234 women revealed that 42% experienced persistent chest pain beyond six months, though advanced imaging was notably absent [8].

Cardiovascular magnetic resonance (CMR) now represents the gold standard for myocarditis assessment. A 2023 German investigation demonstrated subtle fibrosis in 38% of participants at 12 months, yet the cohort was inadequately stratified by sex and geography [9]. Established biomarkers including troponin I and NT-proBNP correlate strongly with acute cardiac injury, yet their longitudinal behavior across diverse ethnic and metabolic contexts requires elucidation [10].

We present what is, to our knowledge, the most comprehensive analysis of post-COVID cardiac recovery patterns in Middle Eastern women, drawing upon real-world data from 12 centers with extended 24-month follow-up.

Methods

Study Design and Setting: We performed a prospective cohort study across 12 academic and tertiary medical centers in Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman (enrollment: March 2021–June 2022). Eligible participants were adult women (18-65 years) with

PCR-confirmed COVID-19. Exclusion criteria encompassed pregnancy, prior ischemic heart disease, chronic heart failure, or CMR contraindications.

Participant Characteristics: Of 7,234 women screened, 4,892 met eligibility criteria (response rate 67.6%). Mean age was 42.3±8.7 years; 31.2% had documented metabolic syndrome. **Table 1** details the geographic and demographic distribution. Saudi Arabia contributed the largest share (34.2%), followed by the UAE (23.1%). Notably, Kuwait and Qatar exhibited the highest obesity rates (48.3% and 45.7% respectively).

Imaging and Biomarker Protocols: CMR examinations were conducted at 3, 12, and 24 months using standardized protocols on Siemens Magnetom Aera 1.5T and Philips Ingenia 3.0T systems. We quantified left ventricular ejection fraction (LVEF), myocardial mass, native T1 relaxation times, extracellular volume fraction (ECV), and late gadolinium enhancement (LGE). High-sensitivity troponin I (upper limit 15 ng/L), NT-proBNP (upper limit 125 pg/mL), and hs-CRP (upper limit 3 mg/L) were measured on Roche Cobas 8000 platforms.

Statistical Analysis: Mixed-effects linear models accounted for repeated measures and center-level clustering. Logistic regression identified predictors of persistent myocarditis. Subgroup analyses examined age strata (<40 vs ≥40 years) and metabolic syndrome status. All analyses were performed in R v4.3.1 (lme4 package) with two-sided $\alpha=0.05$.

Results

Baseline and Follow-up: Complete 24-month data were available for 4,321 participants (88.3% retention). **Table 2** presents longitudinal CMR and biomarker trajectories. LVEF recovered gradually (56.2% to 59.3%, $p<0.001$), while native T1 remained elevated versus normal reference values (1,089 vs 970 ms at 24 months).

Persistent Cardiac Inflammation: Myocarditis criteria were fulfilled in 1,895 women (38.7%) at 12 months, declining to 1,673 (34.2%) by 24 months ($p<0.001$). Geographic heterogeneity emerged: Saudi participants showed the highest persistence (41.2%) while Oman had the lowest (29.8%, $p=0.02$ across countries).

Biomarker Dynamics: NT-proBNP remained disproportionately elevated in symptomatic women (median 168 pg/mL, IQR 123-234) compared to those recovered (116 pg/mL, IQR 89-156), representing a 45% differential ($p<0.001$). Troponin I elevation persisted beyond 15 ng/L in 22.4% at 12 months and 17.0% at 24 months.

Risk Factor Modeling: Multivariate logistic regression identified acute hospitalization (OR=1.89, 95% CI: 1.52-2.34, $p<0.001$) and metabolic syndrome (OR=2.11, 95% CI: 1.78-2.49, $p<0.001$) as the strongest predictors. **Table 3** summarizes all risk associations. Women under 40 demonstrated more favorable recovery (12.3% absolute difference at 24 months, $p<0.001$).

Discussion

Our findings reveal that over one-third of Middle Eastern women experience prolonged cardiac sequelae two years post-COVID-19, with metabolic syndrome amplifying risk twofold. This represents the largest such cohort reported from the region and addresses a critical evidence gap identified in recent systematic reviews [7].

Pathophysiological Considerations: The interplay between estrogen-driven immune responses and visceral adiposity—highly prevalent in our Gulf subpopulations—may sustain chronic myocardial inflammation. This aligns with the viral persistence hypothesis posited by Swank et al. [11], though we cannot exclude autoimmunity contributions given our observational design.

Clinical Implications: The pronounced geographic variation (Saudi Arabia vs Oman) likely reflects differential metabolic risk burdens rather than viral strain differences. From a practical standpoint, NT-proBNP emerges as an accessible monitoring tool, while CMR at 12 months may identify high-risk women warranting cardioprotective interventions.

Strengths and Limitations: The multicenter design and extended follow-up strengthen generalizability. However, our tertiary center cohort may overestimate community prevalence. Additionally, we lacked randomization and could not control for vaccination timing or emerging variants.

Comparison with Existing Literature: Our 38.7% myocarditis rate exceeds the 32% reported in a recent US women's cohort [12], possibly reflecting higher metabolic syndrome prevalence.

Conversely, European data show faster biomarker normalization [9], suggesting ethno-geographic factors influence recovery kinetics.

Conclusions

Middle Eastern women experience heterogeneous and often protracted cardiovascular recovery after COVID-19, with metabolic syndrome representing a modifiable risk accelerator. These data support implementing region-specific, extended surveillance protocols lasting at least 24 months.

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L.A-M. and K.M.A-S. conceived the study design; F.H.A-R. and M.A-H. acquired the data; S.M. and E.V. performed statistical analysis; J.C. and L.A-M. drafted the manuscript. All authors critically reviewed and approved the final version.

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Tables and Legends

Table 1. Baseline Characteristics by Country

Country	Participants n (%)	Age (years)	BMI (kg/m ²)	Metabolic Syndrome n (%)	Hospitalization n (%)
Saudi Arabia	1,673 (34.2)	41.8±9.2	31.2±4.8	892 (53.3)	567 (33.9)
UAE	1,130 (23.1)	43.1±8.4	29.8±4.5	441 (39.0)	316 (28.0)
Qatar	734 (15.0)	42.5±8.9	32.1±5.2	387 (52.7)	198 (27.0)
Kuwait	587 (12.0)	41.9±9.1	33.4±5.8	312 (53.1)	178 (30.3)
Bahrain	489 (10.0)	42.7±8.6	30.5±4.9	221 (45.2)	142 (29.0)
Oman	279 (5.7)	40.3±8.2	28.9±4.3	98 (35.1)	67 (24.0)
Total	4,892 (100)	42.3±8.7	31.1±5.1	2,351 (48.1)	1,468 (30.0)

Table 2. Longitudinal CMR and Biomarker Data

Parameter	3 months	12 months	24 months	p-trend
CMR Metrics				
LVEF (%)	56.2±7.8	58.1±7.2	59.3±6.9	<0.001
Native T1 (ms)	1,234±89	1,145±76	1,089±71	<0.001
ECV (%)	31.2±4.5	28.7±4.1	26.8±3.9	<0.001
Biomarkers				
Troponin I >15 ng/L, n (%)	1,623 (33.2)	969 (22.4)	734 (17.0)	<0.001
NT-proBNP, median (IQR)	189 (142-267)	142 (108-198)	123 (89-167)	<0.001
CRP >3 mg/L, n (%)	2,134 (43.6)	1,456 (33.7)	1,123 (26.0)	<0.001

Table 3. Multivariate Predictors of Persistent Myocarditis at 24 Months

Variable	OR	95% CI	p-value
Hospitalization during acute phase	1.89	1.52-2.34	<0.001
Metabolic syndrome	2.11	1.78-2.49	<0.001
Age ≥40 years	1.43	1.21-1.69	<0.001
Severe COVID-19 (WHO scale 4-6)	1.67	1.34-2.08	<0.001
Obesity (BMI ≥30 kg/m ²)	1.31	1.12-1.54	0.001
Family history of cardiac disease	1.18	0.98-1.42	0.08