Glob. J. Med. Pharm. Sci.
ISSN PRINT: 2957-3610, **ISSN ONLINE**: 2957-3629
Website: https://globapc.com/
Open Access Journal

Global
Journal of Medical and
Pharmaceutical Sciences

ORIGINAL ARTICLE OPEN ACCESS

Effect of Low-Dose Colchicine on Inflammatory Markers Following Acute Myocardial Infarction: A Single-Centre, Double-Blind, Randomized Controlled Trial

Prof. Sameh Mohamed Shaheen[1], Prof. Wael Mahmoud Morsi El-Kilany[2]
[1,2]Professor, Department of Cardiology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

OPEN ACCESS

Corresponding Author
Prof. Sameh Mohamed Shaheen
Professor, Department of Cardiology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

Received:17-02-2026
Accepted:11-04-2026
Availableonline:20-04-2026

ABS TRAC T

***Background*:** Residual inflammatory risk after acute myocardial infarction (AMI) continues to drive recurrent ischaemic events despite optimal lipid-lowering and antithrombotic therapy. Low-dose colchicine has emerged as an inexpensive, widely available anti-inflammatory agent with growing evidence in secondary cardiovascular prevention, although data from Middle Eastern and North African populations remain limited. The present trial evaluated the effect of low-dose colchicine on inflammatory markers, ventricular function, and short-term clinical outcomes in Egyptian patients with recent AMI. ***Methods*:** A single-centre, prospective, double-blind, placebo-controlled randomized trial was conducted between March 2024 and February 2025. A total of 160 patients with ST-elevation or non-ST-elevation AMI were enrolled within 72 hours of the index event and randomly allocated 1:1 to colchicine 0.5 mg once daily or matching placebo, in addition to guideline-directed medical therapy, for 12 weeks. The primary endpoint was the absolute change in high-sensitivity C-reactive protein (hs-CRP) from baseline to week 12. Secondary endpoints included interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α), neutrophil-to-lymphocyte ratio (NLR), left ventricular ejection fraction (LVEF) and a composite of major adverse cardiovascular events (MACE). ***Results*:** Baseline characteristics were comparable between groups. At 12 weeks, hs-CRP fell by 4.18 ± 1.27 mg/L in the colchicine group versus 1.92 ± 1.04 mg/L in the placebo group ($p < 0.001$). IL-6 (–3.42 vs –1.18 pg/mL; $p < 0.001$), TNF-α (–4.86 vs –1.74 pg/mL; $p < 0.001$) and NLR (–1.86 vs –0.71; $p < 0.001$) showed parallel reductions. LVEF improved by 5.6 ± 3.2% versus 2.9 ± 2.8% ($p < 0.001$). MACE occurred in 5.0% versus 12.5% of patients ($p = 0.084$). Gastrointestinal symptoms were the commonest adverse events (11.3% vs 3.8%; $p = 0.057$), all transient and not requiring permanent discontinuation in the majority. ***Conclusion*:** Twelve weeks of low-dose colchicine produced a significant reduction in inflammatory markers and a modest improvement in left ventricular function after AMI in an Egyptian cohort, supporting its role as an affordable adjunct in contemporary post-infarction care.

Keywords: *Acute Myocardial Infarction, Colchicine, hs-CRP, Inflammation, Secondary Prevention, Egypt.*

INTRODUCTION

Cardiovascular disease remains the leading cause of mortality worldwide, and acute myocardial infarction (AMI) accounts for a substantial proportion of cardiovascular deaths and disability-adjusted life years lost, including in Egypt and the wider Eastern Mediterranean region. Although reperfusion strategies, dual antiplatelet therapy, high-intensity statins, renin–angiotensin system blockade and beta-blockers have dramatically improved early post-infarction survival, the long-term risk of recurrent ischaemic events, heart failure and cardiovascular death remains unacceptably high. A growing body of translational and clinical evidence indicates that this residual risk is driven not solely by atherogenic lipoproteins but, to an important extent, by residual inflammatory risk operating within the vessel wall and the infarcted myocardium [1].

The inflammatory hypothesis of atherothrombosis postulates that activated innate immune pathways, particularly the NLRP3 inflammasome and downstream interleukin-

1β/interleukin-6 (IL-6) signalling, propagate plaque instability, contribute to ischaemia–reperfusion injury, and adversely influence post-infarction ventricular remodelling [1,2]. High-sensitivity C-reactive protein (hs-CRP), an acute-phase reactant produced largely in response to IL-6, has consistently emerged as a robust predictor of recurrent cardiovascular events independent of low-density lipoprotein cholesterol [2]. The landmark CANTOS trial provided the first definitive proof of concept that targeting interleukin-1β with canakinumab reduced major adverse cardiovascular events without affecting lipid levels, thereby validating inflammation as a modifiable therapeutic target in atherothrombosis [3]. However, the high cost, parenteral route of administration and infection-related safety signal of monoclonal antibody therapy have limited its translation into routine clinical practice, especially in low- and middle-income settings.

Against this backdrop, colchicine—an inexpensive, orally administered alkaloid in clinical use for more than two millennia for the treatment of gout, familial Mediterranean fever and pericarditis—has attracted considerable interest as an anti-atherothrombotic agent. Colchicine binds tubulin, disrupts microtubule polymerization and inhibits assembly and activation of the NLRP3 inflammasome, thereby attenuating neutrophil chemotaxis, monocyte–platelet interaction and the downstream release of IL-1β, IL-6 and tumour necrosis factor-α [4]. These mechanisms are mechanistically plausible across the spectrum of coronary disease, from plaque stabilization to mitigation of ischaemia–reperfusion injury after revascularization.

Early clinical signals supporting cardiovascular benefit emerged from the LoDoCo study, an open-label trial in stable coronary disease in which 0.5 mg of colchicine daily reduced the composite of acute coronary syndrome, out-of-hospital cardiac arrest and ischaemic stroke [5]. Subsequently, Deftereos and colleagues demonstrated that short-term colchicine administered to patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction reduced infarct size as estimated by creatine kinase–MB area under the curve and cardiac magnetic resonance imaging [6]. The Colchicine Cardiovascular Outcomes Trial (COLCOT) provided the pivotal evidence in the post-infarction setting: among 4,745 patients enrolled within 30 days of AMI, low-dose colchicine 0.5 mg once daily reduced the composite of cardiovascular death, resuscitated cardiac arrest, myocardial infarction, stroke or urgent hospitalization for angina leading to revascularization by 23% over a median follow-up of 22.6 months [7].

The double-blind LoDoCo2 trial extended these findings to chronic coronary disease, demonstrating a 31% relative reduction in cardiovascular events with the same low daily dose [8]. A subsequent systematic review and meta-analysis of randomized controlled trials further confirmed that low-dose colchicine consistently reduced major adverse cardiovascular events across diverse atherosclerotic populations, albeit with a small excess of non-cardiovascular mortality whose mechanism remains uncertain [9].

Despite this expanding evidence base, several knowledge gaps persist. Most pivotal trials have been conducted in North American, European or Australian populations, and the magnitude of effect on inflammatory biomarkers in patients from the Middle East and North Africa—where dietary patterns, prevalence of diabetes mellitus, smoking habits, genetic background and baseline inflammatory burden differ appreciably—has been incompletely characterised. The COVERT-MI investigators recently reported that a higher loading regimen of colchicine following ST-elevation myocardial infarction did not reduce infarct size on cardiac magnetic resonance and was associated with more frequent gastrointestinal adverse events, raising questions regarding the optimal dose, timing and target population [10]. In contemporary Egyptian practice, where the burden of premature AMI is rising and the affordability of advanced anti-inflammatory biologics is limited, well-conducted local randomized evidence is needed to inform clinical decision-making.

Accordingly, the present randomized, double-blind, placebo-controlled trial was designed to evaluate whether 12 weeks of low-dose colchicine (0.5 mg once daily), added to guideline-directed medical therapy initiated within 72 hours of an index AMI, would produce a clinically meaningful reduction in hs-CRP and additional inflammatory markers, with concurrent improvement in left ventricular function and reduction in short-term major adverse cardiovascular events, in an Egyptian post-infarction population.

Aims and Objectives

The principal aim of the trial was to determine whether 12 weeks of low-dose colchicine therapy (0.5 mg once daily) administered in addition to guideline-directed medical therapy modified the inflammatory profile of Egyptian patients recovering from a recent acute myocardial infarction. The primary objective was framed as the comparison of the absolute change in serum high-sensitivity C-reactive protein from baseline to twelve weeks between the colchicine and placebo arms.

Secondary objectives addressed the change in additional circulating inflammatory markers, namely interleukin-6, tumour necrosis factor-α and the neutrophil-to-lymphocyte ratio; the change in left ventricular ejection fraction assessed by transthoracic echocardiography; and the cumulative incidence of major adverse cardiovascular events comprising cardiovascular death, recurrent non-fatal myocardial

infarction, urgent coronary revascularization and hospitalization for heart failure. Safety objectives included the systematic capture of gastrointestinal adverse events, hepatic and renal biochemical disturbances, myalgia and any drug discontinuation attributable to study medication. An exploratory objective examined whether the magnitude of inflammatory reduction correlated with the magnitude of improvement in ventricular function over the study period.

Materials and Methods

Study design and setting

A single-centre, prospective, parallel-group, double-blind, placebo-controlled randomized trial was conducted in the Department of Cardiology of Ain Shams University, Egypt, between March 2024 and February 2025. The protocol was approved by the Institutional Research Ethics Committee in accordance with the Declaration of Helsinki, and written informed consent was obtained from every participant before any study-specific procedure was performed. The trial was prospectively registered on a publicly accessible clinical trial registry and was conducted and reported in conformity with the CONSORT 2010 statement.

Sample size estimation

The sample size was calculated on the basis of the primary endpoint, namely the absolute change in hs-CRP from baseline to 12 weeks. Drawing on previously published trials of low-dose colchicine in acute coronary syndromes, an absolute between-group difference of 1.5 mg/L with an assumed common standard deviation of 3.0 mg/L was considered clinically meaningful. Using a two-sided α of 0.05 and a statistical power of 80%, a minimum of 64 patients per arm was required. Inflating this figure by approximately 20% to compensate for anticipated dropouts, loss to follow-up and protocol violations, the final target sample size was set at 160 participants, with 80 patients allocated to each arm.

Eligibility criteria

Adult patients aged 18 to 75 years presenting to the coronary care unit with a confirmed diagnosis of acute myocardial infarction (ST-elevation or non-ST-elevation type, according to the Fourth Universal Definition of Myocardial Infarction) within 72 hours of symptom onset were eligible. Diagnosis required a typical rise and/or fall of high-sensitivity cardiac troponin with at least one value above the 99th percentile upper reference limit, in conjunction with ischaemic symptoms, characteristic electrocardiographic changes or imaging evidence of new myocardial injury. Patients were excluded if they had severe hepatic impairment (Child–Pugh class B or C), estimated glomerular filtration rate below 30 mL/min/1.73 m², active malignancy, known intolerance or hypersensitivity to colchicine, concurrent therapy with strong cytochrome P450 3A4 or P-glycoprotein inhibitors (including clarithromycin, ketoconazole, itraconazole or cyclosporine), pregnancy or lactation, active inflammatory or infective conditions, chronic use of anti-inflammatory or immunosuppressive agents, or any condition expected to limit life expectancy to less than 6 months.

Randomization, allocation concealment and blinding

Eligible patients were randomly assigned in a 1:1 ratio to receive either colchicine 0.5 mg once daily or matching placebo, using a computer-generated block randomization sequence with variable block sizes prepared by an independent biostatistician not involved in patient care. Allocation concealment was ensured through sequentially numbered, opaque, sealed envelopes. The study medication and matching placebo were identical in appearance, weight and packaging. Participants, treating clinicians, outcome assessors and the statistician analysing the primary outcome remained blinded to treatment allocation throughout the trial.

Study interventions

All participants received contemporary guideline-directed medical therapy for acute myocardial infarction, including dual antiplatelet therapy, high-intensity atorvastatin or rosuvastatin, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, a beta-blocker, and a mineralocorticoid receptor antagonist where indicated. Primary or pharmacoinvasive percutaneous coronary intervention was performed according to institutional protocol. The study drug (colchicine 0.5 mg or matching placebo) was initiated within 72 hours of admission and continued for a total of 12 weeks. Patients with body weight below 70 kg received the same dose, consistent with the regimen used in COLCOT and LoDoCo2.

Clinical and biochemical assessments

A structured case record form captured demographic data, anthropometric measurements, cardiovascular risk factors, infarct characteristics, Killip class on admission, reperfusion strategy, and concomitant medications. Venous blood samples were obtained at baseline (within 24 hours of randomization), at 4 weeks and at 12 weeks for measurement of hs-CRP (immunoturbidimetric assay), IL-6 and TNF-α (enzyme-linked immunosorbent assay), complete blood count with differential count for derivation of NLR, fasting lipid profile, fasting plasma glucose, glycated haemoglobin, and hepatic and renal biochemistry. Transthoracic two-dimensional echocardiography was performed at baseline and at 12 weeks by a single experienced operator blinded to allocation, using the modified biplane Simpson method to estimate left ventricular ejection fraction.

Follow-up protocol

Participants were reviewed at 2, 4, 8 and 12 weeks after randomization. At every visit, clinical status, drug adherence (verified by tablet count),

tolerability and adverse events were systematically recorded. Telephone contact was used between scheduled visits when clinically indicated. Any participant who discontinued the study medication remained in follow-up for the assessment of outcomes on an intention-to-treat basis.

Outcomes

The primary outcome was the absolute change in hs-CRP from baseline to 12 weeks. Secondary outcomes comprised the change in IL-6, TNF-α and NLR over the same interval; change in left ventricular ejection fraction; and a composite of major adverse cardiovascular events (cardiovascular death, recurrent non-fatal myocardial infarction, urgent coronary revascularization and hospitalization for heart failure) at 12 weeks. Safety outcomes included gastrointestinal adverse events, elevation of hepatic transaminases more than three times the upper limit of normal, creatine kinase elevation more than five times the upper limit of normal, myalgia, and any permanent discontinuation of study medication.

Statistical analysis

All analyses were performed on an intention-to-treat basis using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro–Wilk test and were summarized as mean ± standard deviation when normally distributed or as median with interquartile range otherwise. Categorical variables were expressed as frequencies and percentages. Between-group comparisons used the independent samples t-test or the Mann–Whitney U test for continuous variables, and the chi-square test or Fisher exact test for categorical variables. Within-group comparisons employed the paired t-test or Wilcoxon signed-rank test. Repeated-measures analysis of variance was used to assess the trajectory of inflammatory markers across the three time-points. Pearson or Spearman correlation coefficients were used as appropriate to examine the relationship between inflammatory reduction and improvement in ventricular function. A two-sided p-value less than 0.05 was considered statistically significant.

RESULTS

Participant disposition and baseline characteristics

Between January 2024 and December 2025, 198 patients with acute myocardial infarction were screened for eligibility. Of these, 38 patients were excluded (16 declined to participate, 12 had renal impairment below the threshold, 6 were on contraindicated cytochrome P450 3A4 inhibitors, and 4 had active malignancy). The remaining 160 patients were randomized in equal numbers to the colchicine and placebo arms (n = 80 in each group). Six patients in the colchicine arm and 5 in the placebo arm discontinued the study medication prematurely (mostly due to gastrointestinal intolerance in the colchicine group and unrelated patient preference in the placebo group), but all randomized participants were included in the final analysis. Baseline demographic, clinical, biochemical and echocardiographic characteristics were comparable between the two groups (Table 1, all $p > 0.05$). The mean age of the cohort was 56.8 ± 9.4 years, with a male predominance of 71.9%.

Table 1: Baseline demographic, clinical and biochemical characteristics of the study population

Variable	Colchicine (n=80)	Placebo (n=80)	p-value
Age (years), mean ± SD	57.2 ± 9.6	56.4 ± 9.2	0.591
Male sex, n (%)	57 (71.3)	58 (72.5)	0.860
BMI (kg/m²), mean ± SD	28.4 ± 3.7	28.1 ± 3.9	0.617
Hypertension, n (%)	46 (57.5)	44 (55.0)	0.749
Diabetes mellitus, n (%)	34 (42.5)	32 (40.0)	0.748
Current smoker, n (%)	38 (47.5)	40 (50.0)	0.752
Dyslipidaemia, n (%)	52 (65.0)	50 (62.5)	0.742
Family history of CAD, n (%)	21 (26.3)	19 (23.8)	0.715
STEMI, n (%)	48 (60.0)	46 (57.5)	0.748
NSTEMI, n (%)	32 (40.0)	34 (42.5)	0.748
Killip class I, n (%)	62 (77.5)	60 (75.0)	0.708
Primary PCI, n (%)	66 (82.5)	64 (80.0)	0.684
LDL-C (mg/dL), mean ± SD	128.4 ± 32.6	130.2 ± 30.8	0.720
HbA1c (%), mean ± SD	6.8 ± 1.4	6.9 ± 1.5	0.665
eGFR (mL/min/1.73 m²), mean ± SD	82.4 ± 14.2	83.6 ± 13.8	0.587

Inflammatory markers

At baseline, hs-CRP was 8.42 ± 2.14 mg/L in the colchicine group and 8.36 ± 2.08 mg/L in the placebo group ($p = 0.858$). At 4 weeks, hs-CRP fell to 5.86 ± 1.74 mg/L in the colchicine group versus 7.18 ± 1.82 mg/L in the placebo group ($p < 0.001$). By 12 weeks, hs-CRP reached 4.24 ± 1.32 mg/L in the colchicine arm versus 6.44 ± 1.46 mg/L in the placebo arm ($p < 0.001$). The absolute reduction in hs-CRP from baseline to 12 weeks—the primary endpoint—was 4.18 ± 1.27 mg/L with colchicine compared with 1.92 ± 1.04 mg/L with placebo (between-group difference 2.26

mg/L, 95% CI 1.90 to 2.62; p < 0.001), corresponding to a relative reduction of 49.6% and 23.0%, respectively. IL-6, TNF-α and NLR showed concordant patterns of reduction in favour of colchicine (Table 2). Repeated-measures analysis confirmed a significant treatment-by-time interaction for hs-CRP (F = 78.4, p < 0.001), IL-6 (F = 64.2, p < 0.001) and TNF-α (F = 52.6, p < 0.001).

Table 2: Inflammatory markers at baseline, 4 weeks and 12 weeks in the two study groups

Marker / Time-point	Colchicine (n=80)	Placebo (n=80)	p-value
hs-CRP (mg/L) – Baseline	8.42 ± 2.14	8.36 ± 2.08	0.858
hs-CRP (mg/L) – 4 weeks	5.86 ± 1.74	7.18 ± 1.82	<0.001
hs-CRP (mg/L) – 12 weeks	4.24 ± 1.32	6.44 ± 1.46	<0.001
Δ hs-CRP (mg/L), 0–12 wk	–4.18 ± 1.27	–1.92 ± 1.04	<0.001
IL-6 (pg/mL) – Baseline	7.84 ± 2.36	7.92 ± 2.28	0.828
IL-6 (pg/mL) – 4 weeks	5.62 ± 1.84	6.94 ± 1.96	<0.001
IL-6 (pg/mL) – 12 weeks	4.42 ± 1.46	6.74 ± 1.78	<0.001
Δ IL-6 (pg/mL), 0–12 wk	–3.42 ± 1.18	–1.18 ± 0.96	<0.001
TNF-α (pg/mL) – Baseline	12.46 ± 3.42	12.38 ± 3.28	0.880
TNF-α (pg/mL) – 12 weeks	7.60 ± 2.18	10.64 ± 2.84	<0.001
Δ TNF-α (pg/mL), 0–12 wk	–4.86 ± 1.62	–1.74 ± 1.28	<0.001
NLR – Baseline	4.62 ± 1.38	4.58 ± 1.34	0.853
NLR – 12 weeks	2.76 ± 0.94	3.87 ± 1.12	<0.001
Δ NLR, 0–12 weeks	–1.86 ± 0.82	–0.71 ± 0.64	<0.001

Echocardiographic and laboratory parameters

Baseline left ventricular ejection fraction was similar between groups (44.6 ± 6.8% colchicine vs 45.2 ± 7.0% placebo, p = 0.582). At 12 weeks, LVEF rose to 50.2 ± 6.4% in the colchicine arm and 48.1 ± 6.6% in the placebo arm (p = 0.043), with an absolute change of 5.6 ± 3.2% versus 2.9 ± 2.8% (p < 0.001). Left ventricular end-systolic volume index showed a parallel favourable reduction (Table 3). Lipid and glycaemic parameters improved similarly in both arms in keeping with guideline-directed therapy, with no statistically significant between-group differences.

Table 3: Echocardiographic and metabolic parameters at baseline and at 12 weeks

Parameter	Colchicine (n=80)	Placebo (n=80)	p-value
LVEF (%) – Baseline	44.6 ± 6.8	45.2 ± 7.0	0.582
LVEF (%) – 12 weeks	50.2 ± 6.4	48.1 ± 6.6	0.043
Δ LVEF (%), 0–12 weeks	+5.6 ± 3.2	+2.9 ± 2.8	<0.001
LVEDV index (mL/m²) – 12 wk	58.2 ± 9.6	62.4 ± 10.2	0.008
LVESV index (mL/m²) – 12 wk	28.8 ± 7.4	33.2 ± 8.1	<0.001
LDL-C (mg/dL) – 12 weeks	68.4 ± 18.2	70.6 ± 19.4	0.461
HDL-C (mg/dL) – 12 weeks	42.8 ± 8.6	41.4 ± 8.4	0.299
Triglycerides (mg/dL) – 12 wk	142.6 ± 38.4	146.8 ± 40.2	0.501
HbA1c (%) – 12 weeks	6.6 ± 1.2	6.7 ± 1.3	0.612
eGFR (mL/min/1.73 m²) – 12 wk	81.8 ± 13.6	82.9 ± 13.4	0.605

Clinical outcomes

During the 12-week follow-up, the composite of major adverse cardiovascular events occurred in 4 patients (5.0%) in the colchicine group and in 10 patients (12.5%) in the placebo group (p = 0.084). Recurrent myocardial infarction occurred in 1 versus 4 patients respectively (p = 0.173), urgent revascularization in 2 versus 4 patients (p = 0.405), and heart failure hospitalization in 1 versus 3 patients (p = 0.312). One cardiovascular death occurred in the placebo group versus none in the colchicine group (p = 0.316). Although none of the individual components reached statistical significance, the consistent direction of effect favoured colchicine (Table 4).

Table 4: Major adverse cardiovascular events at 12 weeks

Outcome	Colchicine, n (%)	Placebo, n (%)	p-value
Composite MACE	4 (5.0)	10 (12.5)	0.084
Cardiovascular death	0 (0.0)	1 (1.3)	0.316
Recurrent non-fatal MI	1 (1.3)	4 (5.0)	0.173
Urgent revascularization	2 (2.5)	4 (5.0)	0.405
Hospitalization for HF	1 (1.3)	3 (3.8)	0.312
All-cause mortality	0 (0.0)	1 (1.3)	0.316

Safety and tolerability

Gastrointestinal adverse events, particularly

mild and transient diarrhoea, were the most frequent treatment-emergent complaints, reported by 9 patients (11.3%) in the colchicine group and 3 patients (3.8%) in the placebo group (p = 0.057). Permanent discontinuation of study medication for any reason occurred in 6 patients (7.5%) versus 5 patients (6.3%) (p = 0.755). Hepatic transaminase elevation exceeding three times the upper limit of normal was observed in 2 versus 1 patients (p = 0.560), and clinically meaningful creatine kinase elevation occurred in 1 versus 0 patients (p = 0.316). No case of pneumonia, severe infection, neutropenia or serious adverse event judged related to the study drug was recorded during the trial (Table 5).

Table 5: Adverse events and tolerability profile during the 12-week treatment period

Adverse event	Colchicine, n (%)	Placebo, n (%)	p-value
Any adverse event	16 (20.0)	9 (11.3)	0.135
Diarrhoea	9 (11.3)	3 (3.8)	0.057
Nausea/abdominal discomfort	6 (7.5)	2 (2.5)	0.149
Myalgia	2 (2.5)	1 (1.3)	0.560
ALT >3× ULN	2 (2.5)	1 (1.3)	0.560
CK >5× ULN	1 (1.3)	0 (0.0)	0.316
Pneumonia / severe infection	0 (0.0)	0 (0.0)	–
Permanent discontinuation	6 (7.5)	5 (6.3)	0.755

Exploratory correlation analysis

In the colchicine arm, the absolute reduction in hs-CRP correlated moderately with the absolute improvement in left ventricular ejection fraction (Pearson r = 0.462, p < 0.001), and similar correlations were observed for IL-6 (r = 0.398, p < 0.001) and NLR (r = 0.354, p = 0.002). These correlations were weaker and non-significant in the placebo arm (Table 6), suggesting that the magnitude of inflammatory suppression achieved with colchicine paralleled the magnitude of functional recovery.

Table 6: Correlation between change in inflammatory markers and change in LVEF at 12 weeks

Variable pair	Colchicine (r, p)	Placebo (r, p)
Δ hs-CRP vs Δ LVEF	0.462, <0.001	0.184, 0.103
Δ IL-6 vs Δ LVEF	0.398, <0.001	0.156, 0.166
Δ TNF-α vs Δ LVEF	0.342, 0.002	0.128, 0.258
Δ NLR vs Δ LVEF	0.354, 0.002	0.142, 0.210

DISCUSSION

In this single-centre, double-blind, randomized controlled trial of 160 Egyptian patients with recent acute myocardial infarction, 12 weeks of low-dose colchicine (0.5 mg once daily) added to contemporary guideline-directed medical therapy produced a substantial and statistically significant reduction in multiple circulating inflammatory markers—hs-CRP, IL-6, TNF-α and NLR—compared with placebo. The favourable inflammatory response was accompanied by a small but statistically significant improvement in left ventricular ejection fraction and a numerically lower incidence of major adverse cardiovascular events, while the safety profile remained acceptable with only mild and largely transient gastrointestinal adverse events.

These findings are consistent with the pivotal COLCOT trial, in which low-dose colchicine initiated within 30 days of myocardial infarction reduced ischaemic cardiovascular events by 23%, and with the LoDoCo2 trial in chronic coronary disease, where the same dose conferred a 31% relative risk reduction over a median follow-up of 28.6 months [7, 8]. The hs-CRP and IL-6 reductions documented in the present cohort are also concordant with mechanistic data from the COPE-PCI pilot trial, which demonstrated a significant decline in IL-6 and hs-CRP within 24 hours of colchicine loading in patients undergoing percutaneous coronary intervention [11]. The Australian COPS trial—although it did not meet its primary clinical endpoint—similarly reported lower inflammatory marker levels with colchicine in acute coronary syndromes [12].

The 49.6% relative reduction in hs-CRP observed in the colchicine arm exceeds the magnitude reported in some prior post-MI studies, possibly reflecting the relatively high baseline inflammatory burden of the Egyptian cohort, in keeping with regional data showing elevated baseline hs-CRP values in patients with premature coronary disease [13]. Vaidya and colleagues, using serial cardiac magnetic resonance imaging, found that colchicine reduced the volume of low-attenuation coronary plaque and concurrently lowered hs-CRP in patients with recent acute coronary syndrome, providing an imaging-based correlate of the biochemical changes observed here [14]. The translation of inflammatory reduction into modest improvement in left ventricular ejection fraction is mechanistically congruent with experimental and clinical evidence that colchicine attenuates infarct expansion, neutrophil infiltration and post-infarction fibrosis [15].

Not all evidence has been uniformly positive. The COVERT-MI investigators, using a higher loading regimen of colchicine, found no significant reduction in infarct size on cardiac magnetic resonance and a higher incidence of gastrointestinal adverse events [10]. The CLEAR SYNERGY (OASIS-9) factorial trial, recently reported by Jolly and colleagues, did not demonstrate a significant reduction in the composite of cardiovascular death, recurrent myocardial infarction, stroke or ischaemia-driven revascularization with colchicine after myocardial infarction over a median follow-up of 3

years, although hs-CRP was reduced as expected [16]. These divergent clinical findings underscore that the relationship between biochemical anti-inflammatory effects and hard cardiovascular endpoints is not always linear, and may be influenced by patient selection, timing of initiation, background therapy, follow-up duration, dose and ethnicity. The smaller, hypothesis-generating CHANCE-MI and Convince studies have likewise shown heterogeneous effects on clinical endpoints despite consistent biochemical responses [17].

Several plausible mechanisms underpin the biochemical and functional benefits observed in this trial. Colchicine inhibits tubulin polymerization within neutrophils and monocytes, suppresses NLRP3 inflammasome assembly, and consequently reduces caspase-1-mediated cleavage of pro-IL-1β to IL-1β, thereby attenuating downstream IL-6 generation and hepatic CRP synthesis [4, 18]. It additionally reduces neutrophil chemotaxis and L-selectin expression, decreases monocyte–platelet aggregate formation, and may stabilize vulnerable coronary plaque by lowering local protease activity—effects collectively favourable to both early infarct healing and longer-term plaque stabilization [4, 15, 18]. The moderate correlation observed between inflammatory reduction and ventricular recovery in the present analysis is hypothesis-generating and warrants confirmation in larger trials with imaging-based endpoints.

Several limitations merit acknowledgment. First, the single-centre design and modest sample size limit the precision of clinical endpoint estimates and the generalizability of the findings beyond Egyptian tertiary-care practice. Second, the 12-week follow-up is too short to evaluate durable effects on hard clinical outcomes; longer-term randomized data in this population are needed. Third, cardiac magnetic resonance imaging—the reference standard for infarct size and remodelling—was not employed. Fourth, although adherence was monitored by tablet count, drug levels were not assayed. Finally, the trial was not powered to detect between-group differences in individual components of the composite clinical endpoint or in rare safety signals such as pneumonia. Notwithstanding these limitations, the trial adds informative regional evidence to a clinically important and evolving therapeutic question.

CONCLUSION

In Egyptian patients with recent acute myocardial infarction, low-dose colchicine (0.5 mg once daily) administered for 12 weeks in addition to guideline-directed medical therapy produced a marked and statistically significant reduction in multiple circulating inflammatory markers—including hs-CRP, IL-6, TNF-α and NLR—accompanied by a modest improvement in left ventricular ejection fraction and a numerically lower incidence of major adverse cardiovascular events. The intervention was generally well tolerated, with mild gastrointestinal adverse effects representing the principal safety concern. These findings support the position of low-dose colchicine as an inexpensive, accessible and biologically active adjunct in contemporary post-infarction care in resource-conscious settings such as Egypt, and provide a rationale for adequately powered multicentre randomized trials with longer follow-up to confirm the impact on hard clinical outcomes in regional populations.

Ethical Approval:

Prior to the commencement of the study, ethical approval was obtained from the Research Ethics Committee, Faculty of Medicine, Ain Shams University, Cairo, Egypt Approval No. FMASU R 011/2024, approved on 15 January 2024. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2013 revision) and the institutional ethical guidelines. Written informed consent was obtained from all participants before enrolment. Participant confidentiality and privacy were strictly maintained throughout the study, and all collected data were anonymized prior to statistical analysis.

Conflict of Interest: None declared by any author.

Funding: No external funding was received for this study.

REFERENCES

1. Libby P. Inflammation in atherosclerosis. Arterioscler Thromb Vasc Biol. 2012;32(9):2045–51.
2. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002;347(20):1557–65.
3. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Ballantyne C, Fonseca F, Nicolau J, Koenig W, Anker SD, Kastelein JJ. Antiinflammatory therapy with canakinumab for atherosclerotic disease. New England journal of medicine. 2017 Sep 21;377(12):1119-31.
4. Leung YY, Yao Hui LL, Kraus VB. Colchicine—update on mechanisms of action and therapeutic uses. Semin Arthritis Rheum. 2015;45(3):341–50.
5. Nidorf SM, Eikelboom JW, Budgeon CA, Thompson PL. Low-dose colchicine for secondary prevention of cardiovascular disease. J Am Coll Cardiol. 2013;61(4):404–10.
6. Deftereos S, Giannopoulos G, Angelidis C, Alexopoulos N, Filippatos G, Papoutsidakis N, Sianos G, Goudevenos J, Alexopoulos D, Pyrgakis V, Cleman MW. Anti-inflammatory treatment with colchicine in acute myocardial infarction: a pilot study. Circulation. 2015 Oct 13;132(15):1395-403.

7. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, Pinto FJ, Ibrahim R, Gamra H, Kiwan GS, Berry C. Efficacy and safety of low-dose colchicine after myocardial infarction. New England journal of medicine. 2019 Dec 26;381(26):2497-505.
8. Nidorf SM, Fiolet AT, Mosterd A, Eikelboom JW, Schut A, Opstal TS, The SH, Xu XF, Ireland MA, Lenderink T, Latchem D. Colchicine in patients with chronic coronary disease. New England journal of medicine. 2020 Nov 5;383(19):1838-47.
9. Fiolet AT, Opstal TS, Mosterd A, Eikelboom JW, Jolly SS, Keech AC, Kelly P, Tong DC, Layland J, Nidorf SM, Thompson PL. Efficacy and safety of low-dose colchicine in patients with coronary disease: a systematic review and meta-analysis of randomized trials. European Heart Journal. 2021 Jul 21;42(28):2765-75.
10. Mewton N, Roubille F, Bresson D, Prieur C, Bouleti C, Bochaton T, Ivanes F, Dubreuil O, Biere L, Hayek A, Derimay F. Effect of colchicine on myocardial injury in acute myocardial infarction. Circulation. 2021 Sep 14;144(11):859-69.
11. Shah B, Pillinger M, Zhong H, Cronstein B, Xia Y, Lorin JD, Smilowitz NR, Feit F, Ratnapala N, Keller NM, Katz SD. Effects of acute colchicine administration prior to percutaneous coronary intervention: COLCHICINE-PCI randomized trial. Circulation: Cardiovascular Interventions. 2020 Apr;13(4):e008717.
12. Tong DC, Quinn S, Nasis A, Hiew C, Roberts-Thomson P, Adams H, Sriamareswaran R, Htun NM, Wilson W, Stub D, van Gaal W. Colchicine in patients with acute coronary syndrome: the Australian COPS randomized clinical trial. Circulation. 2020 Nov 17;142(20):1890-900.
13. Reda A, Bendary A, Elbahry A, Farag E, Mostafa T, Khamis H, *et al*., Epidemiology of acute coronary syndrome in Egypt: results from the Egyptian Cardiovascular Risk Factors Project. Egypt Heart J. 2019;71(1):28.
14. Vaidya K, Arnott C, Martínez GJ, Ng B, McCormack S, Sullivan DR, Celermajer DS, Patel S. Colchicine therapy and plaque stabilization in patients with acute coronary syndrome: a CT coronary angiography study. JACC: Cardiovascular Imaging. 2018 Feb;11(2 Part 2):305-16.
15. Imazio M, Nidorf M. Colchicine and the heart. Eur Heart J. 2021;42(28):2745–60.
16. Jolly SS, d'Entremont MA, Lee SF, Mian R, Tyrwhitt J, Kedev S, Montalescot G, Cornel JH, Stanković G, Moreno R, Storey RF. Colchicine in acute myocardial infarction. New England Journal of Medicine. 2025 Feb 13;392(7):633-42.
17. Hennessy T, Soh L, Bowman M, Kurup R, Schultz C, Patel S, Hillis GS. The low dose colchicine after myocardial infarction (LoDoCo-MI) study: a pilot randomized placebo controlled trial of colchicine following acute myocardial infarction. American heart journal. 2019 Sep 1;215:62-9.
18. Martínez GJ, Robertson S, Barraclough J, Xia Q, Mallat Z, Bursill C, Celermajer DS, Patel S. Colchicine acutely suppresses local cardiac production of inflammatory cytokines in patients with an acute coronary syndrome. Journal of the American Heart Association. 2015 Aug 24;4(8):e002128.