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File: ■ Pomegranate (*Punica granatum*, Lythraceae)
■ COVID-19
■ Inflammation

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RE: Pomegranate Juice May Improve Inflammatory Status of Adults with COVID-19

Yousefi M, Sadriirani M, Mahmoodi S, et al. Adjuvant pomegranate juice intake improves the inflammatory status of hospitalized COVID-19 patients: A randomized and placebo-controlled trial. *Complement Ther Med*. August 2023;75:102958.
doi:10.1016/j.ctim.2023.102958.

The incubation period for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as COVID-19, can depend on age and health status; the average length is five days. Symptoms include headache, fever, dry cough, fatigue, maldigestion, muscle pain, nausea, and vomiting. Severity can range from mild and moderate to severe and critical. Critical cases can include systemic inflammation, sepsis, and organ dysfunction, all consistent with a cytokine storm. A cytokine storm is a hyperinflammatory syndrome that can cause sudden and fatal hypercytokinemia and multiple organ failure. COVID-19's symptoms, severity, and duration depend on an individual's immune system and nutritional status.

Immune-boosting nutrients are highly recommended to help combat viral infections such as COVID-19. Pomegranate (*Punica granatum*, Lythraceae) contains anthocyanins, flavanols, proanthocyanidins, punicalagins, ellagic acid derivatives, and other organic acids, and it has shown anti-inflammatory properties. Although research has shown potential positive benefits for pomegranate peel extract against COVID-19, there have been no studies with pomegranate juice. The authors therefore conducted a randomized, double-blinded, and placebo-controlled study with a two-arm parallel design to investigate the efficacy of pomegranate juice intake on inflammatory status and complete blood count (CBC) in patients who were hospitalized due to COVID-19.

It was not stated at which hospital or when the trial was conducted; however, it was conducted in Iran. Eligible participants were adults aged > 18 years who were hospitalized with COVID-19 infection that was diagnosed by reverse transcription–polymerase chain reaction test. Ineligible adults were pregnant or lactating, individuals with immunoglobulin A < 61 mg/dL, and those who had disseminated intravascular coagulation or other types of coagulopathies, severe congestive heart failure, or who had participated in any other trial within the past 30 days prior to enrollment.

Pomegranate fruit was picked by hand in Iran, and the juice was obtained by pressing. The juice was pasteurized, concentrated, and filtered, then put into a vacuum bottle and

stored at room temperature until consumption. The placebo contained water with 0.02% pomegranate emulsion prepared by a Mongolia company (Iran) that contained the natural color E-122. The pomegranate juice and placebo appeared and tasted the same. Both groups received 250 mL of product after lunch and dinner daily for 14 days.

A demographic questionnaire was obtained at baseline which included height, weight, body mass index, and blood oxygen saturation. A 24-hour dietary recall was collected for seven days. At baseline and after 14 days, fasting blood samples were obtained to assay interleukin-6 (IL-6), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophils, platelets, lymphocytes, platelet-to-lymphocyte count ratio (PLR), neutrophil-to-lymphocyte count ratio (NLR), blood oxygen saturation (BOS), mean corpuscular volume (MCV), red blood count (RBC) and CBC levels. Each day the length of hospital stay, disease complications, drug and prescription dosing, and mortality rate were recorded. If patients were discharged before the end of the trial, they were followed up after discharge and given the placebo or pomegranate juice. Adherence rate was monitored.

A total of 48 participants were evenly randomized to the pomegranate or placebo group, and 43 completed the study with 21 in the pomegranate group and 22 in the placebo. There was a 90% adherence rate. There were no significant differences in demographics or dietary intake at baseline. The mean age in the pomegranate group was 56.0 ± 11.6 years and 58.6 ± 15.9 years in the placebo.

On day 14, it was found that the pomegranate group saw a significant decrease in IL-6 ($P < 0.001$), CRP ($P < 0.001$), neutrophils ($P < 0.001$), platelets ($P < 0.001$), ESR ($P < 0.001$), PLR ($P = 0.00$), and NLR ($P < 0.001$), and a significant increase in lymphocytes ($P = 0.00$) and BOS ($P < 0.001$) compared to baseline. The placebo group had a significant increase in RBC ($P < 0.001$), lymphocytes ($P = 0.01$), platelets ($P < 0.001$), and BOS ($P < 0.001$) compared to baseline. The pomegranate group had a significantly lower platelet count ($P < 0.001$) and PLR ($P < 0.001$) and a significantly higher MCV ($P = 0.033$) compared to placebo on day 14.

Adverse events were reported in both the placebo group ($n = 5$) and the pomegranate group ($n = 4$). The most common adverse event was nausea and vomiting ($n = 9$).

The authors conclude that pomegranate juice can significantly decrease CRP, IL-6, ESR, neutrophils, platelets, PLR, and NLR levels in patients with COVID-19. Limitations included a small sample size, a short intervention period, not measuring vitamin D levels, not testing the pomegranate juice for the polyphenol content and concentration, and that the results cannot be generalized to all brands of pomegranate juice. More research is needed to verify these results. The authors declare no conflicts of interest.

—*Dani Hoots*

Referenced article can be accessed at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10238276/>.