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Association Between Serum Uric Acid and Vitamin C Levels in Adults With Metabolic Syndrome

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Abstract

Metabolic syndrome (MetS) comprises several interrelated cardiometabolic abnormalities, including central obesity, elevated blood pressure, dyslipidemia, and impaired glucose metabolism. Serum uric acid (SUA) concentrations are frequently elevated in individuals with MetS, while vitamin C is a water-soluble antioxidant that may be associated with urate metabolism. Limited evidence is available concerning the relationship between circulating vitamin C and SUA among Pakistani adults with MetS. This cross-sectional study investigated the correlation between serum vitamin C and SUA and evaluated the association after adjustment for selected cardiometabolic factors. The study was conducted in the Department of Medicine at Hameed Latif Hospital, Lahore, between April and July 2026. A total of 120 adults aged 18–80 years were recruited using consecutive sampling. Demographic, anthropometric, clinical, and biochemical information was obtained. Fasting venous blood samples were collected to measure SUA and serum vitamin C, and dietary vitamin C intake was estimated with a food-frequency questionnaire. Pearson correlation coefficients and multivariable linear regression were used for analysis. The mean age was 49.6 ± 11.2 years, and the mean BMI was 31.4

± 4.7 kg/m². Mean SUA and serum vitamin C concentrations were 6.41 ± 1.38 mg/dL and 0.42 ± 0.18 mg/dL, respectively. Hyperuricemia was identified in 41.7% of participants, while vitamin C deficiency and insufficiency were observed in 28.3% and 46.7%, respectively. Serum vitamin C and SUA were inversely correlated in the total sample ($r = -0.34$, $p < 0.001$), among men ($r = -0.37$, $p = 0.003$), and among women ($r = -0.29$, $p = 0.027$). Following adjustment for age, sex, BMI, blood pressure, triglycerides, HDL cholesterol, and fasting glucose, every 0.1 mg/dL higher serum vitamin C concentration was associated with an estimated 0.19 mg/dL lower SUA (reported coefficient = -0.19 ; 95% CI: -0.28 to -0.10 ; $p < 0.001$). These findings identify a significant inverse association between serum vitamin C and SUA in the selected study population. Because the design was cross-sectional and no treatment was assigned, the findings do not establish a urate-lowering effect of vitamin C. Larger prospective and interventional investigations are needed to clarify the clinical implications.

Keywords: Metabolic Syndrome; Serum uric acid; Vitamin C; Ascorbic acid; Hyperuricemia; Oxidative stress; Metabolic risk factors

1. INTRODUCTION

Metabolic syndrome (MetS) represents a major global public-health challenge and is characterized by a cluster of interrelated cardiometabolic abnormalities, including central obesity, elevated blood pressure, dyslipidemia, and impaired glucose metabolism. Together, these abnormalities substantially increase the risk of developing type 2 diabetes mellitus, cardiovascular disease, and other chronic metabolic conditions. Increasing physical inactivity, unhealthy dietary patterns, and the growing prevalence of obesity have contributed to the burden of MetS across diverse populations. Consequently, identifying associated metabolic markers and potentially modifiable nutritional factors remains an important clinical and public-health priority [1].

The reported prevalence of MetS varies considerably according to diagnostic definitions, population characteristics, and geographic location. In a global meta-analysis involving approximately 28 million adults, Noubiap and colleagues estimated a prevalence ranging from 12.5% to 31.4%, depending on the criteria used to define the syndrome [2]. A systematic review of South Asian populations likewise reported substantial regional variation in the prevalence of MetS, alongside a growing burden of related cardiometabolic disorders [3]. These findings emphasize the importance of investigating metabolic and nutritional factors within particular populations rather than assuming that prevalence estimates or biochemical associations are uniform across regions.

Serum uric acid (SUA) has attracted increasing attention as a potential marker of cardiometabolic dysfunction in individuals with MetS. Elevated SUA concentrations have been associated with obesity, insulin resistance, hypertension, hypertriglyceridemia, and disturbances in glucose metabolism. The relationship is complex and may involve altered renal urate handling, oxidative stress, endothelial dysfunction, low-grade inflammation, and metabolic changes associated with insulin resistance. Higher SUA concentrations may therefore reflect increased cardiometabolic risk, although observational associations cannot, by themselves, establish that uric acid is a causal driver of MetS or cardiovascular disease. The URRAH project provides important evidence concerning associations between uric acid and cardiovascular, renal, and metabolic outcomes [4].

Vitamin C is a water-soluble antioxidant that has attracted considerable interest because of its possible effects on urate metabolism. In a clinical investigation, daily supplementation with 500 mg of vitamin C for two months was associated with reductions in SUA among patients with hyperuricemia, although the response differed among those with gout [5]. These findings suggest a possible urate-lowering effect, but the magnitude, clinical relevance, and durability of that effect remain uncertain across patient groups. Separately, Tetradze and colleagues examined relationships between SUA and metabolic parameters during insulin-sensitizing treatment in patients with MetS; that investigation did not test vitamin C supplementation [6]. A published commentary has also discussed vitamin C supplementation and SUA, but it should be distinguished from an independent intervention trial [7]. Together, these sources provide context for considering both nutritional factors and underlying metabolic disturbances when interpreting SUA.

Population-based investigations provide additional evidence of inverse associations between dietary vitamin C and SUA. An analysis of the US National Health and Nutrition Examination Survey (NHANES) 2011–2016 found that higher dietary vitamin C intake was associated with lower SUA and lower odds of hyperuricemia, with a particularly notable association among men. The adjusted odds ratio for hyperuricemia reported in that analysis was 0.68 (95% CI: 0.57–0.81) for the dietary vitamin C measure studied; this estimate should not be interpreted as the effect of each additional 100 mg/day [8]. A separate NHANES analysis by Zou and colleagues examined dietary vitamin C intake and gout, reporting an inverse association across intake categories and evidence of differences by sex [9]. Although informative, these observational findings do not show that changing vitamin C intake will necessarily reduce uric acid or prevent gout.

More recent experimental research has also examined the relationship between vitamin C status and uric acid concentrations. In the randomized HesperidinC trial, participants with elevated uric acid received interventions involving vitamin C and hesperidin, and the investigators assessed short-term changes in SUA and related metabolic indicators. The study reported a reduction in SUA after one week of 600 mg/day vitamin C supplementation (change: -0.48 ± 0.13 mg/dL, $p < 0.01$). Changes in circulating vitamin C were inversely associated with changes in SUA ($r = -0.25$, $p = 0.03$), and inverse correlations between SUA and plasma vitamin C were also reported after one and two weeks of supplementation ($r = -0.26$, $p = 0.02$, and $r = -0.36$, $p = 0.001$, respectively). Associations involving an index of insulin resistance were additionally reported, suggesting that vitamin C status, urate metabolism, and metabolic regulation may be interrelated [10]. The short observation period and different study population should be considered when comparing these findings with the present research.

Taken together, the available evidence suggests that vitamin C status may be relevant to SUA concentrations in people with metabolic abnormalities. Nevertheless, studies specifically assessing circulating vitamin C and SUA among adults with established MetS in South Asian clinical settings remain limited. The present investigation therefore evaluated this relationship in Pakistani adults with MetS while also considering dietary vitamin C intake and several cardiometabolic characteristics. Examining circulating and dietary indicators within the same population may help clarify the strength

and consistency of the observed associations, identify potentially relevant nutritional patterns, and provide a basis for future prospective or interventional research. Because the design is observational, the findings are intended to describe associations rather than evaluate vitamin C as a treatment.

The objective of this cross-sectional study was to determine the correlation between serum vitamin C and serum uric acid (SUA) concentrations among adults with metabolic syndrome (MetS) and to assess whether this association persisted after adjustment for selected demographic and cardiometabolic factors.

2. METHODOLOGY

A cross-sectional study was conducted in the Department of Medicine at Hameed Latif Hospital, Lahore, Pakistan, between April and July 2026. The sample-size calculation was based on the formula for detecting a Pearson correlation, assuming an expected correlation coefficient of -0.36, and yielded a minimum required sample of 58 participants. To increase the precision of the estimates and provide a larger clinical sample, 120 eligible adults were recruited by non-probability consecutive sampling. Participants were aged 18–80 years and had a diagnosis of metabolic syndrome, as established using the stated clinical diagnostic criteria. Standardized clinical and anthropometric assessments were undertaken, and venous blood was collected following a 12-hour overnight fast for laboratory measurement of SUA and serum vitamin C. Habitual dietary vitamin C intake was assessed using a food-frequency questionnaire (FFQ). Demographic, clinical, anthropometric, and biochemical data were documented on a structured pro forma, entered into Microsoft Excel, and subsequently analyzed using IBM SPSS Statistics, version 28.0.

Eligible participants were men or women aged 18–80 years who fulfilled the study's operational criteria for MetS, were available for clinical assessment and blood collection, could provide dietary information, and gave written informed consent. Eligibility was established using a specified clinical definition of MetS; the precise diagnostic criteria must be reported consistently in the final protocol and manuscript to allow replication and comparisons with other populations.

Exclusion criteria included pregnancy, malignancy, known kidney disease, active infection, and the use of medications likely to affect vitamin C or uric acid metabolism, including diuretics, allopurinol, and febuxostat. Individuals with a reported allergy to vitamin C, those unable to provide sufficiently reliable dietary information, and those who declined to participate were also excluded. These exclusions were intended to reduce the influence of selected clinical conditions and treatments on the measured biochemical associations, although unmeasured sources of confounding could still remain.

After approval from the institutional review board, consecutive potentially eligible patients attending outpatient and inpatient medical services were approached for participation. The study procedures were explained, and written informed consent was obtained before enrollment and collection of study information. A trained research officer used a structured pro forma to record demographics, relevant medical history, current medication use, and clinical characteristics. Height and weight were measured using standardized procedures; body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was recorded at the specified anatomical measurement site, while blood pressure was assessed using an appropriately calibrated instrument after a suitable resting period. Blood samples were collected after overnight fasting for biochemical analysis of SUA and serum vitamin C in the hospital laboratory. Dietary vitamin C intake over the preceding month was estimated using the FFQ. Records were coded, entered into a password-protected electronic database, and prepared for statistical analysis. Participant confidentiality and the right to withdraw were maintained. Reliable interpretation of biochemical measures depends on documenting the laboratory assay, specimen handling conditions, and relevant institutional ethical approvals.

Continuous variables were summarized using means and standard deviations, whereas categorical variables were described using frequencies and percentages. The Shapiro–Wilk test was specified for evaluating the distribution of continuous measurements. Pearson's correlation coefficient was used to estimate the direction and strength of the relationship between serum vitamin C and SUA, both in the overall sample and separately among men and women. Multivariable linear regression was employed to evaluate the association after adjustment for age, sex, BMI, systolic and diastolic blood pressure, triglycerides, high-density lipoprotein (HDL) cholesterol, and fasting glucose. The reported unstandardized coefficient was expressed as the estimated difference in SUA associated with each 0.1 mg/dL increase in serum vitamin C, conditional on the other variables in the model. Additional correlation analyses examined dietary vitamin C intake in relation to circulating vitamin C and SUA. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Analyses were conducted with IBM SPSS Statistics, version 28.0. Given the cross-sectional design, regression coefficients were interpreted as adjusted associations, not estimates of treatment effects or causal reductions in SUA.

3. RESULTS

A total of 120 adults completed the assessments and were included in the analysis. The participants were enrolled in the hospital-based sample according to the stated eligibility criteria, and their baseline characteristics were documented using clinical and laboratory records. Of the 120 participants, 62 (51.7%) were men and 58 (48.3%) were women. The

mean age was 49.6 ± 11.2 years, the mean BMI was 31.4 ± 4.7 kg/m², and the mean waist circumference was 102.8 ± 9.6 cm. These descriptive characteristics indicate that the study involved a middle-aged clinical population with substantial adiposity.

The baseline demographic and anthropometric characteristics are summarized in Table 1. Men accounted for 51.7% of the sample and women for 48.3%, providing a reasonably balanced sex distribution. The overall mean age was 49.6 ± 11.2 years. The mean BMI and waist circumference were 31.4 ± 4.7 kg/m² and 102.8 ± 9.6 cm, respectively. These findings provide the clinical context in which the relationships between vitamin C status, dietary intake, and uric acid concentration were examined.

Table 1. Demographic and anthropometric baseline data for the study population

Parameter	Total (n = 120)
Age (years), mean $\pm$ SD	49.6 ± 11.2
Male, n (%)	62 (51.7%)
Female, n (%)	58 (48.3%)
BMI (kg/m ²), mean $\pm$ SD	31.4 ± 4.7
Waist circumference (cm), mean $\pm$ SD	102.8 ± 9.6

Biochemical characteristics and the distribution of vitamin C status are presented in Table 2. Mean SUA concentration was 6.41 ± 1.38 mg/dL in the overall study sample. The mean concentration was higher among men than women (6.78 ± 1.41 versus 6.02 ± 1.22 mg/dL). Fifty participants, representing 41.7% of the study population, were classified as having hyperuricemia under the study's operational definition. The proportion classified as hyperuricemic depends on the operational uric acid threshold, which should be explicitly defined when these results are compared with reports from other populations.

The mean serum vitamin C concentration was 0.42 ± 0.18 mg/dL. Vitamin C deficiency, defined in the submitted analysis as a concentration below 0.20 mg/dL, was identified in 34 participants (28.3%). A further 56 participants (46.7%) had concentrations between 0.20 and 0.49 mg/dL and were classified as vitamin C insufficient. Overall, 90 of the 120 adults (75.0%) were categorized as deficient or insufficient. These categories were mutually exclusive in the tabulated results. The high proportion with suboptimal serum vitamin C provides a relevant nutritional context for examining the correlation with SUA, although it does not establish the cause or clinical consequences of those low concentrations.

Table 2. Serum vitamin C and uric acid concentrations and vitamin C status in the study population

Parameter	Result
Serum uric acid (mg/dL), mean $\pm$ SD	6.41 ± 1.38
SUA in men (mg/dL), mean $\pm$ SD	6.78 ± 1.41
SUA in women (mg/dL), mean $\pm$ SD	6.02 ± 1.22
Hyperuricemia, n (%)	50 (41.7%)
Serum vitamin C (mg/dL), mean $\pm$ SD	0.42 ± 0.18
Vitamin-C deficiency (<0.20 mg/dL), n (%)	34 (28.3%)
Vitamin-C insufficiency (0.20–0.49 mg/dL), n (%)	56 (46.7%)
Deficient or insufficient vitamin-C status, n (%)	90 (75.0%)

As shown in Table 3, serum vitamin C and SUA concentrations were inversely correlated in the overall study population ($r = -0.34$, $p < 0.001$). The negative coefficient indicates that participants with higher measured serum vitamin C generally had lower measured SUA. The magnitude of this association was moderate rather than strong, and the cross-sectional design does not establish whether vitamin C status directly influences urate metabolism or whether both variables reflect other shared metabolic or dietary factors.

The inverse correlation was also observed when the analysis was stratified by sex. Among men, the reported correlation coefficient was $r = -0.37$ ($p = 0.003$), while among women it was $r = -0.29$ ($p = 0.027$), as presented in Table 3. Both associations were statistically significant at the prespecified threshold and had the same negative direction. The numerically larger coefficient among men should not, however, be taken as evidence of a statistically significant sex difference without a formal comparison or interaction test.

Table 3. Pearson correlations between serum vitamin C and serum uric acid

Analysis	Pearson correlation (r)	p-value
Overall population (n = 120)	-0.34	<0.001
Men (n = 62)	-0.37	0.003
Women (n = 58)	-0.29	0.027

Multivariable linear regression was performed to examine whether the observed relationship between circulating vitamin C and SUA remained after adjustment for selected potential confounders. The covariates specified for adjustment were age, sex, BMI, systolic blood pressure, diastolic blood pressure, triglycerides, HDL cholesterol, and fasting glucose. These variables were selected to account for important demographic and cardiometabolic characteristics that could be related to both vitamin C status and urate concentration. The reported results should be interpreted as conditional associations within the study population rather than as evidence that an intervention to increase vitamin C would produce the estimated reduction in SUA.

Following multivariable adjustment, serum vitamin C remained inversely associated with SUA, as shown in Table 4. Specifically, each 0.1 mg/dL higher serum vitamin C concentration was associated with a 0.19 mg/dL lower SUA concentration (reported coefficient = -0.19; 95% CI: -0.28 to -0.10; $p < 0.001$). The confidence interval excluded zero, indicating statistical evidence of an inverse association under the fitted model. These estimates are conditional on the fitted regression model, and their interpretation depends on the scaling of the vitamin C predictor and the reported adjustment variables.

Table 4. Adjusted linear regression association between serum vitamin C and serum uric acid

Predictor	Regression coefficient	95% CI	p-value
Serum vitamin C (per 0.1 mg/dL increase)	-0.19	-0.28 to -0.10	<0.001

Dietary vitamin C intake was examined in relation to both circulating vitamin C and SUA. These analyses distinguish the reported nutritional exposure estimated by the FFQ from the biochemical measure of circulating vitamin C. Considering both measures is informative because habitual dietary intake and serum concentration are related but not interchangeable indicators of nutritional status. The relevant correlation estimates are presented in Table 5.

As shown in Table 5, dietary vitamin C intake was moderately and positively correlated with serum vitamin C concentration ($r = 0.41$, $p < 0.001$). In contrast, dietary vitamin C intake demonstrated a weaker inverse association with SUA ($r = -0.18$, $p = 0.048$). These findings suggest that reported intake was more closely related to circulating vitamin C than to SUA in this sample. The latter association was close to the conventional threshold for statistical significance, and its small magnitude warrants cautious interpretation, particularly in view of the potential measurement error associated with dietary questionnaires.

Table 5. Correlations of dietary vitamin C intake with serum vitamin C and serum uric acid

Variable	Pearson correlation (r)	p-value
Dietary vitamin-C intake vs. serum vitamin C	0.41	<0.001
Dietary vitamin-C intake vs. SUA	-0.18	0.048

Overall, the results indicate that serum vitamin C was inversely associated with SUA among adults with MetS in the study population, both before and after adjustment for the specified clinical and metabolic covariates. The sex-stratified analyses showed negative associations in both men and women, while the dietary analyses showed a positive relationship between estimated vitamin C intake and serum vitamin C and a weaker negative relationship between intake and SUA. Taken together, these observations are compatible with a relationship between vitamin C status and urate concentrations, but they do not demonstrate that vitamin C supplementation or dietary modification would cause an equivalent reduction in SUA. The high prevalence of vitamin C deficiency or insufficiency also highlights the need for appropriate nutritional assessment and more comprehensive research.

4. DISCUSSION

Metabolic syndrome (MetS) encompasses central obesity, elevated blood pressure, dyslipidemia, and abnormal glucose regulation, all of which contribute to increased cardiometabolic risk. The frequency of MetS varies across age groups, sexes, diagnostic definitions, and geographic populations. Metelskaya and colleagues described the coexistence of its components in an older population, while Noubiap and colleagues documented substantial international variation in prevalence estimates [1, 2]. A review of South Asian populations likewise highlighted the regional burden of MetS and variation across included studies [3]. The present participants were predominantly middle-aged adults with a mean BMI of 31.4 ± 4.7 kg/m², providing an appropriate clinical setting for examining the association of SUA with nutritional indicators. These descriptive characteristics should not, however, be generalized to all Pakistani adults without MetS or to community-based populations.

Serum uric acid is increasingly studied in relation to MetS because disturbances in urate metabolism can coexist with hypertension, obesity, insulin resistance, and renal or cardiovascular abnormalities. The URRAH project emphasized the clinical relevance of hyperuricemia in the context of cardiovascular and kidney disease and metabolic dysregulation [4]. The earlier study by Tetrade and colleagues also examined SUA in patients with MetS during insulin-sensitizing therapy, underscoring the relationship between urate concentrations and metabolic treatment contexts [6]. In the present sample,

mean SUA was 6.41 ± 1.38 mg/dL, and 50 participants (41.7%) were classified as having hyperuricemia. This proportion supports the importance of assessing uric acid in this particular hospital sample, although comparisons with other studies depend on the thresholds used, the composition of the sample, and coexisting clinical conditions.

Vitamin C is an essential water-soluble antioxidant, and its possible influence on urate metabolism has been explored in both observational and intervention studies. Azzeh and colleagues reported changes in SUA following vitamin C supplementation in patients with hyperuricemia or gout, but results differed between the groups and should not be assumed to apply directly to adults with MetS [5]. The commentary by Falsetti and Acciai addresses this research area but does not provide independent trial data [7]. In the present cross-sectional investigation, serum vitamin C showed a moderate inverse correlation with SUA ($r = -0.34$, $p < 0.001$). This means that higher vitamin C concentrations tended to occur alongside lower uric acid concentrations. It does not show that treatment with vitamin C lowered SUA during the study, because supplementation was not assigned and longitudinal changes were not measured.

Evidence from population-based studies provides a relevant comparison. An NHANES 2011–2016 analysis found that higher dietary vitamin C intake was associated with lower SUA and reduced odds of hyperuricemia, with some variation according to sex [8]. Another analysis of American adults reported inverse associations between dietary vitamin C and gout, although that study addressed a different clinical outcome [9]. The present study extends the discussion to adults with established MetS in a Pakistani hospital setting. It also distinguishes dietary intake from circulating vitamin C, reporting a weaker correlation between dietary intake and SUA ($r = -0.18$, $p = 0.048$) than between serum vitamin C and SUA ($r = -0.34$, $p < 0.001$). Differences in dietary assessment, patient selection, outcome definitions, and adjustment for confounding may account for some variation across studies.

The stronger inverse correlation of SUA with measured serum vitamin C than with estimated dietary vitamin C intake may have several explanations. Dietary questionnaires approximate habitual intake and are subject to recall error, portion-size misclassification, and variation in food preparation and nutrient composition. Circulating vitamin C is a biochemical measure that also depends on absorption, distribution, metabolism, recent intake, oxidative stress, and other physiological influences. In the present sample, the positive correlation between dietary intake and serum concentration ($r = 0.41$, $p < 0.001$) supports an expected relationship between these measures without indicating perfect agreement. The randomized HesperidinC trial additionally provides experimental evidence of short-term changes in SUA under a vitamin C-containing intervention [10]. However, the differences in design and population mean that the experimental findings should not be equated with the adjusted observational coefficient reported here.

A substantial proportion of the study population had low serum vitamin C. Specifically, 34 participants (28.3%) were categorized as deficient and 56 (46.7%) as insufficient, giving a combined frequency of 75.0%. These descriptive findings suggest that suboptimal circulating vitamin C status was common in this selected clinical group, but they cannot establish that inadequate dietary intake alone caused the observed concentrations. Oxidative stress and inflammation are relevant features of cardiometabolic disease, although neither mechanism was directly tested as a mediator in this study. Additional indices, including the triglyceride-to-HDL-cholesterol ratio, have been investigated as metabolic markers in other populations [11]. Such complementary indicators may help contextualize biochemical variation in MetS, but were not used here to establish causal pathways linking low vitamin C to hyperuricemia.

The frequency of hyperuricemia also merits consideration in relation to the literature. A study of adults in Pakistan identified demographic and metabolic factors associated with elevated SUA [12]. Separate clinical research has described hyperuricemia among patients with hypertension [13], while a survey in Sukkur documented its occurrence in a regional Pakistani population [14]. The present frequency of 41.7% was obtained specifically among adults with MetS attending a hospital; the denominators, diagnostic thresholds, and background characteristics may therefore differ substantially from those in other reports. For this reason, the estimate should be described as a prevalence within the selected study sample rather than a population-wide estimate for Pakistan. The findings nevertheless support further investigation of SUA in relation to nutritional and cardiometabolic characteristics.

The positive relationship between dietary and serum vitamin C is also relevant to evaluating nutritional assessment methods. Food-frequency questionnaires are designed to characterize habitual dietary exposure, and a pilot validation study by Santosh and David examined an FFQ specifically intended to estimate vitamin C consumption [15]. The particular questionnaire used in the present study should be identified so that its validation status and suitability for Pakistani dietary patterns can be assessed. Recall error, uncertainty regarding portions, seasonal availability, and losses of vitamin C during storage or cooking may contribute to differences between dietary estimates and measured concentrations. Accordingly, serum vitamin C should not be treated as an exact proxy for dietary intake, and dietary estimates should not be interpreted as direct evidence that changing intake would alter SUA by a predictable amount.

MetS is a multifactorial condition involving several interacting physiological pathways rather than a single biochemical abnormality. Alongside glucose dysregulation, obesity, and lipid abnormalities, other biomarkers may indicate aspects of the underlying metabolic environment. For example, a consensus statement on metabolic hyperferritinemia described how abnormal ferritin concentrations can coexist with metabolic dysfunction and emphasized the importance of clinical

context in their interpretation [16]. Although ferritin was not analyzed as a central variable in this investigation, the broader literature illustrates the complexity of biochemical changes accompanying MetS. This context reinforces the need for caution when attempting to attribute the relationship between serum vitamin C and SUA to one biological mechanism without prospective observations or direct mechanistic measurements.

Further evidence connects urate metabolism with the broader pathophysiology of MetS, although whether uric acid has a direct causal role remains uncertain. Copur and colleagues reviewed possible mechanisms linking uric acid with features of metabolic syndrome and discussed the limitations of existing evidence [17]. In the present study, the inverse association between serum vitamin C and SUA persisted after adjustment for age, sex, BMI, systolic and diastolic blood pressure, triglycerides, HDL cholesterol, and fasting glucose. The reported coefficient indicates that each 0.1 mg/dL higher serum vitamin C concentration corresponded to an estimated 0.19 mg/dL lower SUA (95% CI: -0.28 to -0.10; $p < 0.001$). This suggests that the measured covariates did not fully account for the observed statistical association, but it does not exclude residual confounding, measurement error, reverse causation, or unmeasured dietary and renal factors.

Observational research has examined whether dietary and circulating vitamin C are associated with MetS more broadly. A meta-analysis by Guo and colleagues reported inverse associations between both measures of vitamin C and MetS across the included studies [18]. Similarly, analysis of Korean national nutrition-survey data found that a dietary pattern rich in calcium and vitamin C was inversely associated with MetS risk [19]. The relatively high frequency of suboptimal serum vitamin C in the present sample and its inverse association with SUA are consistent with this broader research direction. Nevertheless, these other studies address the occurrence of MetS, whereas all participants in the current analysis already had MetS and the principal outcome was SUA concentration. The findings are therefore complementary rather than directly interchangeable. The cross-sectional design also precludes conclusions about the temporal order of vitamin C depletion and urate accumulation.

Intervention studies provide a separate line of evidence concerning potential biological effects. In a meta-analysis of 16 randomized controlled trials involving 1,013 participants, Liu and colleagues found that oral vitamin C supplementation was associated with a reduction in SUA; the observed effects varied according to trial characteristics, including intervention duration and participant age [20]. These experimental findings make the observational association biologically plausible, but do not establish that supplementation would have the same effect in the current Pakistani hospital sample. Participants with MetS may differ from trial participants in dietary intake, comorbid conditions, renal urate handling, and medication exposure. Furthermore, the present study did not assign vitamin C treatment, assess change over time, or record clinical outcomes attributable to supplementation. Thus, the findings should not be presented as an efficacy study or as justification for substituting vitamin C for established therapy.

Sex-stratified analyses showed that the inverse association between serum vitamin C and SUA was present in both men ($r = -0.37$, $p = 0.003$) and women ($r = -0.29$, $p = 0.027$). Both coefficients were negative, and the association was numerically stronger among men. However, without a statistical interaction test or a formal comparison of the two independent correlation coefficients, it would be premature to conclude that the relationship truly differs by sex. Differences in body composition, dietary behavior, hormonal characteristics, renal urate handling, and medication use are possible explanations that would require direct assessment. The key observation supported by the present data is that an inverse relationship was detected in both groups rather than being confined to only one sex.

The study has several strengths that are relevant to its primary objective. It included both a biochemical measurement of serum vitamin C and an estimate of habitual dietary vitamin C intake, allowing these complementary indicators to be considered together. SUA was assessed alongside several major clinical and cardiometabolic characteristics, and multivariable regression was used to account for selected measured covariates. The sex-stratified correlation analyses provide an additional descriptive assessment of the consistency of the association. Finally, the positive correlation between dietary intake and circulating vitamin C supplies internal evidence of a relationship between exposure and biochemical status, although it does not independently validate the questionnaire or eliminate measurement error. These features strengthen the descriptive interpretation of the observed associations while leaving questions of causality unresolved.

Several limitations must be considered. First, the cross-sectional design does not establish temporal sequence or causality between serum vitamin C and SUA. Second, consecutive recruitment from hospital services may limit generalizability to the wider Pakistani population, including individuals with MetS who do not seek hospital care. Third, FFQ estimates are vulnerable to recall error, inaccurate portion-size estimation, differences in food composition, and variation in preparation methods. Fourth, SUA is influenced by factors such as renal function, dietary purines, fructose intake, alcohol exposure, hydration, and medication use; some of these may not have been completely measured or adjusted for. Fifth, serum vitamin C assays can be sensitive to specimen handling, and full laboratory-method details are not provided in the submitted text. Sixth, the operational definitions of MetS, hyperuricemia, and vitamin C insufficiency require clear documentation. Although the regression model included important covariates, residual confounding and model misspecification cannot be excluded. Accordingly, the results cannot estimate the effect of increasing vitamin C intake or supplementation on SUA.

In summary, the study identified an inverse association between circulating vitamin C and SUA among adults with MetS

receiving care in a Pakistani hospital. This relationship was evident in both sexes and remained statistically significant after adjustment for the specified demographic and cardiometabolic variables. Dietary vitamin C intake was positively associated with serum vitamin C and more weakly inversely associated with SUA. The substantial proportion of participants classified as vitamin C deficient or insufficient highlights the potential importance of nutritional assessment in this population. However, these findings concern observed associations and do not demonstrate that increasing vitamin C intake causes uric acid concentrations to fall. Prospective cohort studies and adequately powered randomized trials with clearly defined clinical endpoints are needed to investigate whether correcting low vitamin C status influences SUA or broader metabolic outcomes.

5. CONCLUSION

Among 120 adults with metabolic syndrome, serum vitamin C showed a statistically significant inverse correlation with serum uric acid. The association was detected in both men and women and persisted after adjustment for age, sex, BMI, systolic and diastolic blood pressure, triglycerides, HDL cholesterol, and fasting glucose. Approximately three-quarters of the participants had serum vitamin C concentrations classified as deficient or insufficient, indicating that suboptimal vitamin C status was frequent in this hospital-based sample. Dietary vitamin C intake was positively correlated with circulating vitamin C and weakly inversely correlated with SUA. These observations support the hypothesis that circulating vitamin C status is associated with SUA among adults with MetS, but they do not establish causation or demonstrate the benefits of vitamin C treatment. Given the observational design and limited geographic setting, vitamin C supplementation cannot be recommended as a replacement for established management of hyperuricemia or metabolic syndrome on the basis of these data. Larger prospective studies and carefully designed randomized controlled trials are needed to determine whether correcting vitamin C deficiency produces sustained changes in SUA and improves metabolic or cardiovascular outcomes.

Author contributions

All authors contributed equally to the conception, development, preparation, and revision of the manuscript. All authors reviewed and approved the final version of the manuscript.

Conflict of interests

The authors declare that they have no conflicts of interest.

Data availability

The study generated participant-level clinical and biochemical data. Requests for access to de-identified data may be directed to the corresponding author and would require applicable institutional permissions, appropriate safeguards for participant confidentiality, and compliance with ethical requirements.

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