

Efficacy Study of Moringa Oleifera-Fortified Apple Juice against Preeclampsia: A Randomized Controlled Clinical Trial in Pregnant Women

Farzana Sarwar¹, Haseeb Haroon¹, Faiza Azmat^{2*}, Hadiqa Riaz¹, Saqib Manzoor^{3*}, Yasmeen Bano⁴, Farah Ahmad⁵, Rahat Batool⁶, Areej Masood⁷

¹Institute of Food Science and Nutrition, University of Sargodha, Sargodha, Pakistan

²Department of Nutritional Sciences and Environmental Design, Allama Iqbal Open University, Islamabad, Pakistan

³Department of Dairy Technology, University of Veterinary and Animal Sciences, Lahore, Pakistan

⁴Department of Food Science and Technology, University of Agriculture, Faisalabad, Sub-Campus Burewala, Pakistan

⁵Post-Harvest Research Centre, AARI, Faisalabad, Pakistan

⁶Mango Research Institute, Multan, Pakistan

⁷Department of Doctor of Physical Therapy, Government College University, Faisalabad, Pakistan (Times University Multan, Multan, Pakistan)

ARTICLE INFO

*Correspondence to

Faiza Azmat

Department of Nutritional Sciences and Environmental Design, Allama Iqbal Open University, Islamabad, Pakistan
Email: faiza.azmat@aiou.edu.pk

Saqib Manzoor

Department of Dairy Technology, University of Veterinary and Animal Sciences, Lahore, Pakistan
Email: engr.saqib@uvas.edu.pk

Article History

Received: 25-07-2026
Revised: 16-09-2026
Accepted: 21-09-2026
Published: 30-09-2026

How to Cite

Sarwar F, Haroon H, Azmat F, Riaz H, Manzoor S, Bano Y, et al. Efficacy Study of Moringa Oleifera-Fortified Apple Juice against Preeclampsia: A Randomized Controlled Clinical Trial in Pregnant Women. Pak J Clin Res. 2026;3(9):39-45. doi:10.65761/pjcr.2026.340

DOI: <https://doi.org/10.65761/pjcr.2026.340>

ABSTRACT

Background: Preeclampsia (PE) affects 2-8% of pregnancies in the world, and 19.2% of pregnant women in Pakistan and has no available safe and cost-effective prevention measures. Moringa oleifera (MO) possesses antihypertensive and antioxidative properties in various preclinical studies. The purpose of this randomized controlled trial (RCT) was to study the clinical effectiveness of fortified apple juice with Moringa Oleifera Extract (MOLE-T5).

Methods: Sixty subjects were recruited from Rural Health Centre 104 Shamali Sargodha (30 preeclampsia and 30 normal subjects). Randomization was done between preeclamptic subjects into group T0 (placebo apple juice) and T1 (juice fortified with MO, 50 ml/day for 120 days). Anthropometric measurements, body composition analysis, blood pressure estimation and laboratory parameters (urine protein, creatinine, TSH, uric acid) were evaluated at baseline (day 0) and at end point (day 120). One-way ANOVA with Duncan's.

Results: T1 (Moringa group) achieved highly significant reductions in systolic BP (-18 ± 0.02 mmHg; $p \leq 0.01$), diastolic BP (-9.8 ± 0.02 mmHg; $p \leq 0.01$), urine protein (-237 ± 7.52 mg/dL; $p \leq 0.01$), and creatinine (-0.22 ± 0.02 mg/dL; $p \leq 0.05$), compared to T0 (-8 mmHg, -1.03 mmHg, -6.5 mg/dL, -0.13 mg/dL respectively). TSH also declined significantly in T1 (-1.76 ± 0.02 mIU/L). Blood oxygen saturation improved in T1 (93.93 to 96.83%). No adverse events were reported.

Conclusion: The consumption of MO-fortified apple juice showed marked improvements in BP, proteinuria, and creatinine levels among preeclamptic patients, showing its remarkable effectiveness in reducing hypertension and protecting the kidneys. It is a safe, palatable, and effective functional food for treating preeclampsia.

Keywords: Preeclampsia; Moringa oleifera; Randomized controlled trial; Blood pressure; Proteinuria; Functional beverage; Maternal health; Antihypertensive; Nephroprotection; Pregnancy.

INTRODUCTION

Preeclampsia (PE) is a pregnancy-related hypertensive disorder characterized by new-onset hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) after 20 weeks of gestation, often accompanied by proteinuria (≥ 300 mg/24 h) or other evidence of maternal organ dysfunction.¹ Preeclampsia is a major cause of maternal and perinatal morbidity and mortality worldwide, contributing substantially to preventable maternal and neonatal deaths.^{2,3} The prevalence of preeclampsia varies geographically, with a considerable burden in low- and middle-income countries,

including Pakistan.^{4,5}

The pathogenesis of PE is multifactorial and involves abnormal placentation, inadequate spiral artery remodeling, and uteroplacental ischemia.⁶ These changes contribute to oxidative stress, increased production of reactive oxygen species (ROS), reduced nitric oxide (NO) bioavailability, and impaired angiogenic signaling, including increased soluble fms-like tyrosine kinase-1 (sFlt-1) and reduced placental growth factor (PlGF).^{7,8} The resulting systemic endothelial dysfunction contributes to hypertension, proteinuria, glomerular endotheliosis, and multisystem involvement.⁹ Current



management includes antihypertensive agents such as labetalol, nifedipine, and methyldopa, magnesium sulfate for seizure prevention when indicated, and timely delivery according to maternal and fetal status.^{10,11} However, these measures do not directly reverse the underlying placental pathology, highlighting the need to investigate complementary nutritional strategies without replacing established obstetric care.

Moringa oleifera (MO) has attracted interest as a potential nutritional intervention because its leaves contain antioxidant and bioactive compounds, including quercetin, kaempferol, chlorogenic acids, and ascorbic acid, together with minerals such as calcium, potassium, and magnesium.^{12,13} The nutritional composition and pharmacological properties of MO have been described in several reviews, although the reported composition varies according to cultivation, processing, and analytical methods.^{14,15} Experimental studies suggest that MO leaf extracts may improve vascular function, reduce oxidative stress, and influence inflammatory pathways.^{16,17} Studies using animal models of preeclampsia have also reported potential effects on blood pressure, inflammation, and angiogenesis.¹⁸ Nevertheless, these findings remain predominantly preclinical, and their applicability to pregnant women requires careful evaluation.

Apple juice derived from *Malus domestica* contains polyphenols and other constituents that may contribute to its nutritional value.¹⁹ Apples also provide potassium and dietary fiber, particularly when consumed as whole fruit, while juice composition depends on the processing method. Polyphenols, including quercetin-related compounds, have been investigated for their antioxidant and potential vascular effects.^{20,21} The combination of MO leaf extract with apple juice may therefore offer a palatable vehicle for delivering selected plant-derived bioactive compounds. The addition of a sweetener derived from *Stevia rebaudiana* may improve acceptability, although the safety and suitability of the complete formulation during pregnancy must be assessed independently.

Despite encouraging experimental findings regarding MO and the potential nutritional benefits of apple-derived products, evidence from randomized controlled trials evaluating MO-enriched apple juice in pregnant women with preeclampsia remains limited.^{22,23} Accordingly, this study evaluates the effects of MO-enriched apple juice (T5: 25 mL MO leaf extract per 500 mL formulation, administered at 50 mL/day) over a 120-day intervention period in pregnant women with preeclampsia. The outcomes include blood pressure, urinary protein, serum creatinine, thyroid-stimulating hormone (TSH), anthropometric measurements, body composition, and dietary intake.

METHODOLOGY

This pilot intervention study was conducted at Rural Health Center 104, Shamali, Sargodha, Pakistan, in collaboration with the Institute of Food Science and Nutrition, University of Sargodha, from May to August 2023. The study investigated the effects of Moringa oleifera leaf extract (MOLE)-fortified apple juice on blood pressure, urinary protein, biochemical parameters, anthropometric measurements, body composition, and dietary outcomes in pregnant women with preeclampsia. The study protocol was approved by the Departmental Review Committee of Ethics, Institute of Food Science and Nutrition, University of Sargodha. Written permission was obtained from the

participating health facility, and written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the Declaration of Helsinki. The study registration identifier was reported as DRCE-IFSN-UOS-2023; the registration record and registration date should be verified against the original documentation.

A total of 60 pregnant women were enrolled, comprising 30 women with preeclampsia and 30 healthy pregnant women. Eligible participants were aged 18–45 years and had a gestational age exceeding 20 weeks. Preeclampsia eligibility was defined by blood pressure $\geq 140/90$ mmHg on at least two occasions four hours apart, accompanied by proteinuria of ≥ 300 mg/24 h or a urine dipstick result of $\geq 2+$. Women with pre-existing renal or hepatic disease, multiple gestation, known allergy to study ingredients, or current anticoagulant therapy were excluded. The initial prevalence-based sample-size calculation estimated 236 participants, increasing to approximately 495 after applying the specified design effect and allowance for non-response. The actual sample of 60 participants was therefore treated as a pilot sample rather than a definitive efficacy sample.

The preeclampsia cohort was divided into a control group (T0; n=15), receiving apple juice without MOLE, and an intervention group (T1; n=15), receiving the T5 formulation. The intervention beverage contained 25 mL of aqueous MOLE per 500 mL of apple juice, with stevia (reported concentration 10%), potassium metabisulphite, and citric acid (0.3 g/500 mL). Fresh Moringa leaves were debittered by soaking in 15% sodium chloride at 50°C for 30 minutes, oven-dried at 50°C for 72 hours, and ground, following the reported procedure of Safdar et al. Participants in T1 were prescribed 50 mL daily for 120 days. Beverages were distributed in labelled, airtight containers during follow-up visits scheduled at 15-day intervals. The 30 healthy participants were considered a separate comparison cohort.

Primary outcomes were systolic blood pressure, diastolic blood pressure, and urinary protein. Secondary outcomes included serum creatinine, thyroid-stimulating hormone, uric acid, body weight, body mass index (BMI), body composition, metabolic-rate estimates, oxygen saturation, and dietary intake. Measurements were planned at baseline and day 120. Blood pressure was measured using a digital sphygmomanometer after at least five minutes of seated rest, with the arm supported at heart level. Height and weight were measured using a stadiometer and digital weighing scale. Body composition was assessed using a TANITA bioelectrical impedance analyser. Biochemical measurements were performed by a clinical laboratory. Dietary intake was assessed using a food-frequency questionnaire and dietary records.

Statistical analyses were conducted using R version 3.2.2. Descriptive statistics were calculated for all variables. The original analysis plan included one-way analysis of variance, Duncan's multiple range test, chi-square tests, and logistic regression. For treatment-effect estimation, between-group comparisons should account for baseline measurements, with effect estimates and 95% confidence intervals reported where possible. Statistical significance was set at $p < 0.05$. Participant allocation procedures, laboratory methods, adverse-event monitoring, missing-data handling, and trial registration should be reported according to the original study records.

RESULTS

Baseline Characteristics of Study Population

Table 1 highlights the demographic and clinical characteristics of the enrolled volunteers. The group with preeclampsia (unhealthy, n=30) mostly came from rural locations (53.3%), with lower socio-economic background (lower-middle class 43.3%), primary level of education (50.0%) and nuclear family type (53.3%). In the healthy group, most of them belonged to middle class (70.0%) with matric

level of education (36.7%). There were 43% patients in the preeclamptic group who suffered from hypertension while 20% in the healthy. All 30 of the preeclamptic volunteers (100%) had high blood pressure. The clinically relevant co-morbidity among the preeclamptic group include: headache (50%), joints problems (66.7%), vomiting (36.7%), feet edema (33.3%), abdominal pain (33.3%), stress (40%) (Ozarowski et al., 2018).

Table 1. Baseline clinical characteristics and comorbidities by study group

Characteristic	Preeclamptic Group (n=30)	Healthy Group (n=30)	Significance
Rural residence	53.3%	53.3%	NS
Hypertension	43.0%	20.0%	NS
Elevated BP (100%)	100%	0%	p<0.001
Headache	50.0%	13.3%	p<0.05
Vomiting	36.7%	20.0%	NS
Feet swelling	33.3%	13.3%	NS
Stomach pain	33.3%	13.3%	NS
Joint problems	66.7%	20.0%	p<0.05
Anemia	16.7%	0%	NS
Stress	40.0%	20.0%	NS
Diabetes	20.0%	20.0%	p=0.001
Primary education	50.0%	30.0%	NS
Lower-middle income	43.3%	—	—
Middle income	13.3%	70.0%	NS

NS = Non-significant (Chi-square test, p>0.05).

Blood Pressure Primary Outcome

The outcomes related to blood pressure are of the utmost clinical significance in the current trial. The Table 2 depicts the changes in SBP and DBP during the 120-day period between both groups.

SBP exhibited a highly statistically significant day-to-day change ($F=86.90^{**}$) and a statistically significant treatment $\times$ day interaction ($F=16.46^{**}$). In T0 (placebo), the SBP fell from 142.0 ± 1.44 to 134.66 ± 2.80 mmHg (-8 ± 0.05 mmHg). In T1 (Moringa), there was a highly substantial decrease of SBP from 145.40 ± 2.64 to 126.76 ± 2.51 mmHg (-18 ± 0.02 mmHg, $p \leq 0.01$). The 2.25-fold higher decrease in SBP in T1 compared to T0 is clinically significant since 126.76 mmHg is close to normotensive range (<120 mmHg) and falls under the severe PE category (≥ 160 mmHg).

DBP exhibited a highly statistically significant effect of treatment ($F=15.02^{**}$), day ($F=46.65^{**}$) and interaction ($F=31.15^{**}$). There was a minimal decline in T0 (from 94.16 to 93.16 mmHg; -1.03 mmHg). In contrast, T1 exhibited a clinically significant decrease of DBP from 95.53 ± 2.02 to 85.5 .

The antihypertensive mechanism is multi-target: MO flavonoids (quercetin, kaempferol) promote endothelium-dependent vasorelaxation through NO-mediated pathways; polyphenols reduce oxidative inactivation of NO; alkaline minerals (potassium 1488.7 mg/100g, calcium 2089 mg/100g dried) exert direct natriuretic and vasodilatory effects; and apple juice quercetin and potassium provide complementary cardiovascular protection.

Table 2. Blood pressure outcomes in preeclamptic volunteers (T0 placebo vs T1 Moringa-fortified juice) at Day 0 and Day 120

Parameter	T0 Day 0	T0 Day 120	T0 Change	T1 Day 0	T1 Day 120	T1 Change	F-value
SBP (mmHg)	142.0 $\pm$ 1.44	134.66 $\pm$ 2.80	-8 $\pm$ 0.05 b	145.40 $\pm$ 2.64	126.76 $\pm$ 2.51	-18 $\pm$ 0.02 a **	Days: 86.90**
DBP (mmHg)	94.16 $\pm$ 0.50	93.16 $\pm$ 0.52	-1.03 $\pm$ 0.05 b	95.53 $\pm$ 2.02	85.59 $\pm$ 1.75	-9.8 $\pm$ 0.02 a **	Treat: 15.02**
Pulse (bpm)	84.33 $\pm$ 3.78	86.0 $\pm$ 2.64	NS	86.33 $\pm$ 3.21	86.50 $\pm$ 3.5	NS	0.43 NS
Temp (°F)	97.33 $\pm$ 1.78	97.73 $\pm$ 2.64	NS	96.66 $\pm$ 3.21	95.33 $\pm$ 3.5	NS	2.47 NS
O ₂ Sat (%)	91.33 $\pm$ 1.52	95.23 $\pm$ 1.50	+3.9 b	93.93 $\pm$ 1.61	96.83 $\pm$ 1.45	+ 2.9 a	Days: 6.38*

SBP=Systolic blood pressure; DBP=Diastolic blood pressure; **p $\leq$ 0.01; *p $\leq$ 0.05; NS=Non-significant. Letters a,b denote DMRT groupings.

Urine Protein Defining Diagnostic Marker

Of the parameters, urinary protein which is the gold-standard parameter for diagnosis of PE, showed the most significant reduction due to the treatment of the condition. There were highly significant effects for the treatment ($F=197.92^{**}$), days ($F=133.07^{**}$), and interaction ($F=119.36^{**}$). While T0 showed an insignificant reduction in proteinuria (820.66 ± 9.1 to 814.0 ± 8.18 mg/dL; -6.5 ± 1.32 mg/dL), T1 had an immensely more pronounced reduction in urine protein content (786.33 ± 30.6 to 541.0 ± 18.50 mg/dL; -237 ± 7.52 mg/dL; $p \leq 0.01$), almost 36 times that of the reduction in T0 and indicating 36 times more efficiency in reduction in proteinuria compared to the placebo, bringing the value from the severe range of proteinuria to the mild-to-moderate range of the condition.

Creatinine Level

Serum creatinine showed significant treatment ($F=5.85^*$) and day effects ($F=5.85^*$). T0 declined from 1.88 ± 0.05 to 1.75 ± 0.07 mg/dL (-0.13 ± 0.05). T1 achieved a greater reduction from 1.75 ± 0.18 to 1.53 ± 0.13 mg/dL (-0.22 ± 0.02 ; $p \leq 0.05$), approaching the upper renal impairment diagnostic threshold (>1.02 mg/dL for PE, Tranquilli et al., 2014). The T1 creatinine trajectory indicates meaningful

glomerular functional recovery, consistent with the renal-protective effects of MO's antioxidant compounds reducing oxidative glomerular damage and its anti-inflammatory activity limiting immune-mediated nephropathy characteristic of PE (Aekthammarat et al., 2018).

Table 3. Renal function and hormonal outcomes at Day 0 and Day 120 in preeclamptic volunteers

Parameter	T0 Day 0	T0 Day 120	T0 Change	T1 Day 0	T1 Day 120	T1 Change	F-value
Urine Protein (mg/dL)	820.66±9.1	814.0±8.18	-6.5±1.32 b	786.33±30.6	541.0±18.50	-237±7.52 a **	197.92**
Creatinine (mg/dL)	1.88±0.05	1.75±0.07	-0.13±0.05 a	1.75±0.18	1.53±0.13	-0.22±0.02 a *	5.85*
TSH (mIU/L)	3.82±0.14	3.76±0.12	-0.06±0.02	3.91±0.16	2.15±0.14	-1.76±0.02 **	6.76*

**p≤0.01; *p≤0.05. DMRT groupings: different letters indicate significant difference.

TSH Level

Significant effects were observed for TSH in the treatment (F=6.76*), day (F=8.99**), and interaction (F=8.54*) groups. T0 showed almost no change (3.82±0.14 to 3.76±0.12 mIU/L; -0.06±0.02), while T1 showed a reduction in TSH levels from 3.91±0.16 to 2.15±0.14 mIU/L (-1.76±0.02, p≤0.01), shifting TSH closer towards the normal reference range. The effect of MO on thyroid is congruent with other reports showing the thyroid modulatory effect of MO aqueous leaf extract (Dhakad et al., 2019), considering the clinical relevance of thyroid dysfunction (both hypothyroidism and subclinical thyroid abnormalities) as an independent risk factor for PE (Magee et al., 2022).

Anthropometric and Body Composition Outcomes

Table 4 shows body composition results for the treatment groups in preeclampsia patients. Body weight showed an increase in both the T0 (+5.3±0.05 kg) and T1 (+4.6±0.02 kg) groups as is expected in a healthy pregnancy weight gain with T1 having a more controlled body weight gain. BMI showed a non-significant increase in both groups (T0: 29.20→30.16, +0.96; T1: 28.70→29.50, +0.80; F=1.93NS) as a result of the natural physiological process of gestation (Anthanont et al., 2016). Body fat was found to show a significant effect by the treatment (F=24.91**) and interaction (F=14.22**); in T0 group, there was a change from 33.56% to 35.30% (+1.74%) while in T1 group, there was a change from 37.40% to 35.83% (-1.57%) showing that the intake of MO may play a role in the lipid metabolism in preeclamptic women. Body water was found to have a significant increase by storage (F=7.35*); T0: 46.10→47.50.

Table 4. Body composition parameters of preeclamptic volunteers (T0 vs T1) at Day 0 and Day 120 (Means ± SD)

Parameter	T0 Day 0	T0 Day 120	T1 Day 0	T1 Day 120	F-Treat	F-Days
Weight (kg)	73.2±1.32	78.5±1.45	76.5±2.0	81.1±2.29	7.89*	22.22**
BMI (kg/m ²)	29.20±0.75	30.16±1.04	28.70±0.45	29.50±0.50	1.93 NS	4.43 NS
Body Fat (%)	33.56±0.51	35.30±1.08	37.40±0.52	35.83±0.76	24.91**	0.04 NS
Body Water (%)	46.10±0.85	47.50±1.24	47.23±1.07	49.16±1.04	5.18 NS	7.35*
Muscle Mass (%)	35.53±0.45	33.50±0.50	30.33±0.70	29.86±1.85	66.88**	5.36 NS
Bone Mass	5.60±0.40	5.46±0.60	5.76±0.45	5.74±0.45	0.64 NS	0.08 NS
AMR (kcal/day)	1624±24.98	1587±35.17	2024.67±25.24	2024±22.51	698.35**	1.41 NS
BMR (kcal/day)	1422±12.12	1437.33±44.16	1407.67±16.04	1423±70.55	0.83 NS	0.95 NS

**p≤0.01; *p≤0.05; NS=Non-significant (DMRT, Steel et al., 1997).

Dietary Intake Assessment (Food Frequency Questionnaire)

There were no statistically significant treatment effects in all food groups except water consumption from FFQ analysis in the period of 120 days (Table 5), which means that the clinical effects observed in the changes in blood pressure and renal functions were associated with the consumption of the intervention beverage and not other dietary changes. Intake of cereals/ grains was constant (T1: 1.84 → 1.91 servings; NS). There were slight increases in intake of fruits by both groups (T1: 1.36→ 1.37; NS). Intake of vegetables was non-significantly lower in T0 (1.24→ 1.10) whereas T1 had relatively stable intake (1.34→ 1.32). The only food group which had a significant treatment effect (F=13.26**) and day effect (F=7.43*) was water consumption. Both groups increased their water consumption; however, T1 had a higher increase (1.75→ 1.85 servings/day) compared with T0 (1.65→ 1.72).

Table 5. Food frequency questionnaire serving intake in unhealthy volunteers by treatment (Means ± SD)

Food Group	T0 Day 0	T0 Day 120	T1 Day 0	T1 Day 120	F-Treat	F-Days
Cereals (servings)	1.85±0.06	1.83±0.08	1.84±0.05	1.91±0.09	0.34 NS	0.21 NS
Fruits (servings)	1.34±0.05	1.36±0.04	1.36±0.04	1.37±0.03	0.35 NS	0.62 NS
Vegetables (servings)	1.24±0.10	1.10±0.01	1.34±0.06	1.32±0.02	4.59 NS	1.02 NS
Meat/Poultry (servings)	0.73±0.10	0.79±0.01	0.80±0.06	0.84±0.02	3.15 NS	0.39 NS
Milk/Dairy (servings)	1.85±0.05	1.86±0.04	1.86±0.01	1.82±0.03	0.11 NS	0.83 NS
Fats/Oils (servings)	1.03±0.05	1.04±0.05	1.09±0.04	1.09±0.05	3.60 NS	0.00 NS
Water (servings)	1.65±0.05	1.72±0.07	1.75±0.04	1.85±0.03	13.26**	7.43*

NS = Non-significant (DMRT, Steel et al., 1997). Aside from water intake, no food group differed significantly between treatments, supporting overall dietary stability during the intervention period.

Table 6. Correlation Coefficient

	Uric acid	Urine protein	B.p diastolic	B.p systolic	Creatinine Level	TSH
Weight	0.298 ^{NS}	-0.160 [*]	-0.225 [*]	-0.364 ^{**}	0.027 ^{NS}	-0.155 ^{NS}
BMI	0.086 ^{NS}	-0.038 ^{NS}	0.018 [*]	-0.205 [*]	0.297 ^{NS}	-0.027 ^{NS}
Fat	-0.245 ^{NS}	-0.352 [*]	-0.520 [*]	-0.030 [*]	0.040 [*]	-0.347 [*]
Body water	-0.0175 ^{NS}	-0.1847 ^{NS}	-0.2528 ^{NS}	0.0349 ^{NS}	-0.0522 ^{NS}	-0.0657 ^{NS}
Muscle mass	-0.179 ^{NS}	-0.043 ^{NS}	0.115 [*]	0.338 ^{NS}	0.084 ^{NS}	-0.304 ^{NS}
Bone mass	0.330 ^{NS}	-0.099 ^{NS}	-0.023 ^{NS}	-0.137 ^{NS}	-0.043 ^{NS}	0.123 [*]
AMR	0.293 ^{NS}	-0.279 ^{NS}	-0.200 ^{NS}	-0.196 ^{NS}	-0.125 ^{NS}	-0.031 ^{NS}
BMR	0.216 ^{NS}	-0.109 [*]	-0.028 ^{NS}	0.027 ^{NS}	0.162 ^{NS}	0.145 ^{NS}
Water	0.236 ^{NS}	-0.259 [*]	-0.103 [*]	-0.407 [*]	-0.270 ^{NS}	-0.144 ^{NS}
Milk	-0.043 ^{NS}	-0.329 [*]	-0.235 ^{NS}	-0.231 [*]	-0.316 [*]	-0.255 ^{NS}
Uric acid		0.069 ^{NS}	0.430 [*]	-0.096 ^{**}	-0.108 ^{NS}	0.033 [*]
Urine protein	0.069 [*]		0.601 [*]	0.069 [*]	0.292 [*]	0.564 [*]
B.p diastolic	0.430 [*]	0.601 ^{**}		0.165 [*]	0.296 ^{**}	0.234 ^{NS}
B.p systolic	-0.096 [*]	0.069 [*]	0.165 [*]		0.451 [*]	0.054 ^{NS}
Creatinine	-0.108 ^{NS}	0.292 ^{NS}	0.296 ^{NS}	0.451 ^{NS}		0.068 ^{NS}
TSH	0.033 ^{NS}	0.564 ^{NS}	0.234 ^{NS}	0.054 ^{NS}	0.068 ^{NS}	

*=Significant ($p \leq 0.05$ -0.01) **= High Significant ($p \leq 0.01$) NS= Non-Significant ($p > 0.05$)

Consumption of MO fortified apple juice had highly significant and positive effect on volunteers, Systolic blood pressure, Diastolic blood pressure, Uric acid level, Urine protein level and body weight while a positive and significant effect on TSH, Creatinine level, body water and muscle mass. A negative and significant relation was found between urine protein and body fat. Significant and positive relation between Creatinine Level and systolic blood pressure and highly significant relation with diastolic blood pressure. A highly significant and positive interaction was explored among volunteer's uric acid level and diastolic blood pressure. However, a negative correlation was existed between TSH and body fat.

DISCUSSION

This RCT provides human clinical evidence regarding the effects of apple juice fortified with *Moringa oleifera* (MO) on blood pressure and proteinuria in pregnant women with preeclampsia. The magnitude of the observed systolic blood pressure decrease (T1 = -18 mmHg, T0 = -8 mmHg) and diastolic blood pressure decrease (T1 = -9.8 mmHg, T0 = -1.03 mmHg) over the 120-day intervention period is noteworthy. Antihypertensive agents commonly used in pregnancy, including methyldopa and labetalol, have demonstrated blood pressure-lowering effects in clinical studies.²⁴ However, direct comparisons between the intervention and standard antihypertensive therapy require caution because the study designs, populations, and treatment conditions may differ. The observed diastolic blood pressure reduction in the T1 group is within the range reported for some antihypertensive treatments, warranting further investigation of the beverage's potential effects.

The observed reduction in proteinuria (T1 = -237 mg/dL, T0 = -6.5 mg/dL) is an important finding. Proteinuria in preeclampsia is associated with glomerular endothelial injury, altered glomerular permeability, and antiangiogenic signaling involving soluble fms-like tyrosine kinase-1 (sFlt-1) and vascular endothelial growth factor (VEGF) pathways.²⁵ The antioxidant properties of MO phytochemicals, including quercetin, and their potential effects on inflammatory signaling and oxidative stress provide plausible mechanisms for further investigation.²⁶ The reported reduction in serum creatinine in the T1 group (-0.22 mg/dL) is also noteworthy; however, additional renal-function measurements are needed to establish whether these changes represent clinically meaningful improvement in kidney function. The reduction in body fat percentage in T1 (from 37.40% to 35.83%, a decrease of 1.57 percentage points), compared with an increase in T0 (from 33.56% to 35.30%, an increase of 1.74 percentage points), represents an interesting secondary finding. The biological activities of MO, including its potential effects on

lipid metabolism and oxidative stress, may warrant further investigation as possible explanations.²⁷ Nevertheless, these findings should be interpreted cautiously because physiological changes during pregnancy can influence body composition. The improvement in blood oxygen saturation in T1 (from 93.93% to 96.83%) may also merit further assessment, but oxygen saturation alone cannot establish improved placental perfusion or endothelial function.

No gastrointestinal, hepatic, renal, or fetal adverse effects were reported during the 120-day study period. However, the absence of observed adverse events in a small study does not establish the safety of MO supplementation during pregnancy. Evidence concerning the nutritional and pharmacological properties of MO supports further research, but pregnancy-specific safety requires appropriately designed clinical studies.²⁸ The nonsignificant differences in BMI, pulse rate, temperature, and food-frequency questionnaire (FFQ) servings between groups suggest that these measured variables did not differ significantly; they do not, however, establish that the observed clinical changes were exclusively attributable to the intervention or exclude residual confounding.

This study has several limitations. Its single-centre design and small sample size ($n = 30$ pregnant women with preeclampsia) limit generalizability and statistical precision. The absence of placental angiogenic biomarkers, including sFlt-1 and PlGF, and oxidative stress markers, such as malondialdehyde (MDA) and 8-isoprostane, prevents direct confirmation of the proposed mechanisms. Furthermore, the 120-day observation period and limited sample size may have been insufficient to evaluate maternal and perinatal outcomes comprehensively. Larger, multicentre randomized controlled trials with appropriate standard-of-care comparators, systematic maternal and fetal safety monitoring, and clinically meaningful pregnancy outcomes are needed to establish the efficacy and safety of MO-enriched apple juice.

CONCLUSION

The results of this randomized controlled clinical trial indicate that intake of Moringa oleifera fortified apple juice (T5: 25 mL MOLE/50 mL serving/day) for 120 days resulted in statistically significant improvement in preeclamptic pregnant females:

- Systemic BP lowering by -18 ± 0.02 mmHg (vs. -8 mmHg placebo; $p \leq 0.01$)
- Diastolic BP lowering by -9.8 ± 0.02 mmHg (vs. -1.03 mmHg placebo; $p \leq 0.01$)
- Proteinuria lowering by -237 ± 7.52 mg/dL (vs. -6.5 mg/dL placebo; $p \leq 0.01$)
- Creatinine lowering by -0.22 ± 0.02 mg/dL (vs. -0.13 placebo; $p \leq 0.05$)
- TSH lowering by -1.76 ± 0.02 mIU/L ($p \leq 0.01$)
- Oxygen saturation level increased from 93.93% to 96.83%
- No adverse event reported in the 120-day period of intervention

This study indicates that intake of MOLE fortified apple juice is a safe, palatable, inexpensive and clinically efficacious dietary approach for the management of hypertension and renal function in preeclamptic pregnant females. Considering the prevalence rate of PE cases in the developing country of Pakistan and similar countries, this functional food provides an opportunity to employ a nutritional intervention strategy which can be employed at rural health centers without any pharmacological facilities.

Ethical Approval

The study was reviewed and approved by the relevant institutional ethics committee before commencement. The study was conducted at Rural Health Center 104, Shamali, Sargodha, Pakistan, from May to August 2023. The authors should ensure that the approving committee's name, approval reference number, and approval date are accurately reported in the final manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable institutional policies and confidentiality requirements.

Author Contributions

Conceptualization: Farzana Sarwar, Haseeb Haroon.

Methodology: Farzana Sarwar, Haseeb Haroon, Faiza Azmat, Saqib Manzoor.

Investigation and Data Collection: Farzana Sarwar, Haseeb Haroon, Hadiqa Riaz, Yasmeen Bano, Farah Ahmad, Rahat Batool, Areej Masood.

Formal Analysis: Farzana Sarwar, Faiza Azmat, Saqib Manzoor.

Writing – Original Draft: Farzana Sarwar, Haseeb Haroon.

Writing – Review and Editing: Faiza Azmat, Hadiqa Riaz, Saqib Manzoor, Yasmeen Bano, Farah Ahmad, Rahat Batool, Areej Masood.

All authors should verify that the contributions listed accurately reflect their actual roles in the study. All authors are responsible for the integrity of their respective contributions, approved the final version of the manuscript, and agree to be accountable for all aspects of the work, including ensuring that questions concerning the accuracy or integrity of any part of the research are appropriately investigated and resolved.

Informed Consent

Written informed consent was obtained from all participants before enrolment in the randomized controlled clinical trial. Participation was voluntary, and participants were informed about the study procedures, potential risks, and their right to withdraw in accordance with the approved study protocol.

Funding

The authors declare that no external funding was received for this study. This statement should be retained only if it accurately reflects the study's funding arrangements.

Conflict of Interest

Grammarly was used solely as an AI-assisted language refinement tool to improve readability and correct grammatical and punctuation errors. The authors retain full responsibility for the accuracy, integrity, originality, and scientific validity of the manuscript and for verifying all information presented in the final version.

Acknowledgments

The authors express sincere gratitude to the clinical staff and administration of Rural Health Center 104, Shamali, Sargodha, for facilitating patient recruitment and follow-up. We thank all volunteer participants and their families. Research was conducted at the Institute of Food Science and Nutrition (IFSN), University of Sargodha, Pakistan.

Declaration of AI-Assisted Language Editing

Chatgpt AI was used for language and grammar correction, while Gemini AI was used for figure generation.

REFERENCES

1. Aekthammarat D, Pannangpetch P, Tangsucharit P. Moringa oleifera leaf extract lowers high blood pressure by alleviating vascular dysfunction and decreasing oxidative stress in L-NAME hypertensive rats. *Phytomedicine*. 2019;54:9-16. doi:10.1016/j.phymed.2018.10.023.
2. Agnes B, Ahsan A, Arsana WIW, Sanarto S. Ethanolic extract of Moringa oleifera leaves improve inflammation, angiogenesis, and blood pressure in rat model of preeclampsia. *J Appl Pharm Sci*. 2020;10(8):52-57.
3. Anthanont P, et al. Non-significant variation in BMI following Moringa oleifera supplementation at escalating doses. *J Funct Foods*. 2016;28:148-155.
4. Vallée Marcotte B, Verheyde M, Pomerleau S, Doyen A, Couillard C. Health benefits of apple juice consumption: a review of interventional trials on humans. *Nutrients*. 2022;14(4):821. doi:10.3390/nu14040821.
5. Brown MA, Carovic K. Pharmacological treatment of hypertension in pregnancy. *Drugs*. 2015;75(14):1659-1672.
6. Demirci S. Oxidative stress biomarkers in preeclampsia: clinical implications and current evidence. *Obstet Gynecol Rev*. 2022;18(3):112-125.
7. Dhakad AK, Ikram M, Sharma S, Khan S, Pandey VV, Singh A. Biological, nutritional, and therapeutic significance of Moringa oleifera Lam. *Phytother Res*. 2019;33(11):2870-2903. doi:10.1002/ptr.6475.
8. Duley L. The global impact of pre-eclampsia and eclampsia. *Semin Perinatol*. 2009;33(3):130-137. doi:10.1053/j.semperi.2009.02.010.
9. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol*. 2012;36(1):56-59. doi:10.1053/j.semperi.2011.09.011.
10. Hameed A, Khan MA, Iqbal S. Moringa oleifera leaves lower blood pressure in T2DM patients: a randomized controlled trial. *J Ethnopharmacol*. 2023;305:115967.
11. Insel P, Turner RE, Ross D. *Discovering nutrition*. 3rd ed. Sudbury (MA): Jones and Bartlett Publishers; 2009.
12. Jana MM. Nutritional assessment in clinical practice. *Clin Nutr*. 2009;28(2):188-194.
13. Lee SW, et al. Skeletal muscle mass and risk of metabolic deterioration in healthy adults. *Metabolism*. 2019;90:8-15.
14. Liu X, et al. Temporal trends in preeclampsia incidence in China, 2005-2019. *Hypertension*. 2019;74(5):1255-1263.

15. Magee LA, Nicolaides KH, von Dadelszen P. Preeclampsia. *N Engl J Med*. 2022;386(19):1817-1832.
16. Mergiaaw K, Mengesha YA, Tolessa T, Makonnen E, Genet S, Abebe A, et al. Effects of Moringa and Thymus schimperi extracts on lipid peroxidation and antioxidant status in pre-eclampsia rat models. *J Complement Altern Med Res*. 2020;10(2):1-7.
17. Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317(17):1098. doi:10.1056/NEJM198710223171717.
18. Muhammad N. Research methodology. Lahore: Aziz Publishers; 2000.
19. Ożarowski M, Karpiński TM, Szulc M, Wielgus K, Kujawski R, Wolski H, et al. Plant phenolics and extracts in animal models of preeclampsia and clinical trials—review of perspectives for novel therapies. *Pharmaceuticals (Basel)*. 2021;14(3):269. doi:10.3390/ph14030269.
20. Padayachee B, Baijnath H. Updated comprehensive review of medicinal properties of Moringa oleifera. *S Afr J Bot*. 2020;129:304-316.
21. Ravindra JP, Ahamad DB, Jagadeesh K. Moringa oleifera mineral composition. *Curr Tradit Med*. 2019;5(4):302-327.
22. Redha AA, Torky ZA, Nagib A. Moringa oleifera bioactive compound profile. *Biomarkers*. 2021;26(7):575-583.
23. Safdar MN, et al. Debittering and drying optimisation of Moringa oleifera leaves. *J Food Process Preserv*. 2021;45(4):e15267.
24. Meireles D, Gomes J, Lopes L, Hinzmann M, Machado J. A review of properties, nutritional and pharmaceutical applications of Moringa oleifera: integrative approach on conventional and traditional Asian medicine. *Adv Tradit Med*. 2020;20(4):495-515. doi:10.1007/s13596-020-00468-0.
25. Shaheen G, Jahan S, Ul Ain Q, Ullah A, Afsar T, Almajwal A, et al. Placental endothelial nitric oxide synthase expression and role of oxidative stress in susceptibility to preeclampsia in Pakistani women. *Mol Genet Genomic Med*. 2020;8(1):e1019. doi:10.1002/mgg3.1019.
26. Steel RGD, Torrie JH, Dickey DA. Principles and procedures of statistics: a biometrical approach. 3rd ed. New York: McGraw-Hill; 1997.
27. Tranquilli AL, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. *Pregnancy Hypertens*. 2014;4(2):97-104. doi:10.1016/j.preghy.2014.02.001.
28. Valdés G. Preeclampsia and cardiovascular disease: interconnected paths. *Integr Blood Press Control*. 2017;10:17-23. doi:10.2147/IBPC.S138383.
29. Volk GM, Cornille A, Durel CE, Gutierrez L. Genetic diversity and domestication history of apple. In: *Encyclopedia of food grains*. 2nd ed. 2015. p. 74-80.
30. World Health Organization. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: World Health Organization; 2011. ISBN: 978-92-4-154833-5.