ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081

Journal of Medical & Health Science Review

IMPACT OF POMEGRANATE-DERIVED ANTIOXIDANTS ON HAEMATOLOGICAL PARAMETERS IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

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ARTICLE INFO

Keywords

Pomegranate, Antioxidants, Iron Deficiency Anaemia, Haematological Parameters, Randomized Controlled Trial

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ABSTRACT

Iron deficiency anaemia (IDA) is a prevalent nutritional disorder characterized by inadequate iron availability, frequently resulting in impaired haemoglobin synthesis and reduced oxygen transport. Conventional iron supplementation, the primary treatment modality, is often associated with challenges such as poor patient compliance due to gastrointestinal side effects and suboptimal iron absorption, thus limiting its overall effectiveness. Recent evidence suggests that adjunctive therapies involving antioxidants, such as those abundantly found in pomegranate (*Punica granatum*), may offer a promising approach to enhance iron absorption, mitigate oxidative stress, and improve haematological parameters in anaemic patients. This study aimed to investigate the impact of pomegranate-derived antioxidants on key haematological parameters in patients diagnosed with IDA. A randomized, controlled trial (RCT) was conducted, involving 60 adult participants with confirmed IDA. Participants were randomly assigned to either the intervention group, receiving 250 mL of pomegranate juice daily in addition to standard oral iron therapy, or the control group, receiving oral iron therapy alone. The intervention period lasted for 8 weeks, with haematological parameters including haemoglobin levels, serum ferritin, and mean corpuscular volume measured at baseline, 4 weeks, and 8 weeks. The results of this study suggest that pomegranate-derived antioxidants may serve as a valuable adjunctive treatment strategy, potentially improving haematological outcomes in IDA patients compared to standard iron therapy alone. This highlights the potential of incorporating antioxidant-rich foods like pomegranate into the therapeutic regimen for IDA to improve overall patient outcomes. Further research is warranted to elucidate the underlying mechanisms and long-term benefits of this approach.

INTRODUCTION

Iron deficiency Anaemia (IDA) remains a pressing global health challenge, affecting a significant proportion of the population, particularly women of reproductive age, pregnant women, and young children (1). As the most prevalent form of Anaemia worldwide, IDA is characterized by insufficient iron to meet the body's needs, leading to reduced haemoglobin production and impaired oxygen delivery to tissues (2). The consequences of IDA extend beyond fatigue and weakness, impacting cognitive function, immune response, and overall quality of life (3)(4). The pathophysiology of IDA is multifaceted, involving inadequate dietary intake, impaired iron absorption, increased iron requirements during growth or pregnancy, and chronic blood loss (5). Diagnostic criteria typically include low haemoglobin levels, reduced serum ferritin concentrations, and decreased mean corpuscular volume (MCV) (6). While iron supplementation is the cornerstone of IDA treatment, it is often plagued by several limitations, including poor patient compliance due to gastrointestinal side effects such as nausea, constipation, and abdominal discomfort (8). Moreover, the bioavailability of oral iron supplements can be affected by dietary factors, interactions with other medications, and underlying gastrointestinal conditions, leading to suboptimal absorption and treatment outcomes (9). In light of these challenges, there is a growing interest in exploring complementary and alternative strategies to enhance iron absorption, mitigate oxidative stress, and improve overall haematological parameters in individuals with IDA. Recent studies have highlighted the potential role of antioxidants, including those derived from fruits and vegetables, in modulating iron metabolism and reducing the adverse effects of iron deficiency (10). Pomegranate (*Punica granatum*) is a fruit renowned for its rich antioxidant content, attributed to its high concentration of polyphenolic compounds such as anthocyanins, flavonoids, ellagic acid, and tannins (11). These bioactive compounds have demonstrated potent antioxidant, anti-inflammatory, and cardioprotective properties in various in vitro and in vivo studies (12). The antioxidant properties of pomegranate are hypothesized to play a crucial role in improving iron absorption by reducing the formation of insoluble iron complexes, enhancing iron bioavailability, and protecting against oxidative damage to red blood cells (12). Several studies have investigated the potential benefits of pomegranate consumption on haematological parameters in different populations. For instance, a study by (13) reported that pomegranate juice supplementation improved haemoglobin levels and red blood cell indices in elderly individuals with mild Anaemia. Similarly, a study by (14) found that pomegranate juice consumption increased haemoglobin levels and serum ferritin concentrations in pregnant women with IDA. Furthermore, research suggests that pomegranate extracts may protect against iron-induced oxidative stress and inflammation in animal models (15). Given the potential benefits of pomegranate-derived antioxidants in improving iron metabolism and reducing oxidative stress, the present study aimed to evaluate the impact of pomegranate juice consumption on haematological parameters, including haemoglobin (Hb), serum ferritin, mean corpuscular volume (MCV), and red blood cell (RBC) count, in patients with iron deficiency Anaemia. We hypothesized that pomegranate juice supplementation, as an adjunct to standard iron therapy, would result in significant improvements in haematological parameters and a reduction in fatigue symptoms compared to iron therapy alone. The findings of this study may provide valuable insights into the potential role of pomegranate as a complementary strategy in the management of IDA. The aim of the study is to assess the impact of pomegranate-derived antioxidants on haemoglobin levels in patients with iron deficiency Anaemia, and examine changes in serum ferritin, mean corpuscular volume (MCV), and red blood cell (RBC) count and to assess the improvements in quality of life and fatigue scores among participants.

Material and Methods

Study Design: A **randomized controlled trial** (RCT) performed in Al-Sehat Hospital Timergara and was conducted with two groups: one receiving pomegranate juice as an adjunct to iron therapy and the other receiving only standard iron therapy. The study was double-blinded, with participants and researchers unaware of group assignments.

Participants: The study enrolled 60 participants, aged 18-45 years, who were diagnosed with iron deficiency Anaemia based on the following criteria:

- Haemoglobin (Hb) <12 g/dL for women and <13 g/dL for men.

- Serum ferritin levels <30 ng/mL.
- No history of chronic illnesses like cardiovascular disease, gastrointestinal disorders, or chronic kidney disease.

Exclusion Criteria:

- Pregnancy or lactation.
- Any allergic reaction to pomegranate.
- Concurrent use of antioxidant supplements or medications affecting iron metabolism.

Intervention: Participants were randomly assigned to one of two groups:

- **Group A (Control):** Received 100 mg of oral iron supplement daily.
- **Group B (Intervention):** Received 100 mg of oral iron supplement daily, along with 250 mL of pomegranate juice containing 200 mg of antioxidant polyphenols.

The intervention lasted 8 weeks, with haematological parameters measured at baseline, 4 weeks, and 8 weeks.

Data Collection: Blood samples were collected at baseline, 4 weeks, and 8 weeks to measure:

- Haemoglobin (Hb) concentration (g/dL)
- Serum ferritin (ng/mL)
- Mean corpuscular volume (MCV) (fL)
- Red blood cell (RBC) count ($\times 10^6/\mu L$)

In addition, participants completed the Fatigue Severity Scale (FSS) to evaluate subjective fatigue levels.

Statistical Analysis: Data were analysed using SPSS statistical software. Paired t-tests were used to compare pre- and post-intervention values within each group. Independent t-tests were used to compare changes between the intervention and control groups. A significance level of $p<0.05$ was considered statistically significant.

Results: The results represents a comprehensive analysis of the data collected during the 8-week randomized controlled trial. The primary aim was to assess the impact of pomegranate-derived antioxidants, as an adjunct to standard iron therapy, on haematological parameters in patients with iron deficiency Anaemia (IDA). The results are presented under specific headings, with supporting figures and tables to illustrate the key findings.

Baseline Characteristics

The study enrolled 60 participants, with 30 individuals randomly assigned to each group: a control group receiving standard iron therapy and an intervention group receiving standard iron therapy plus 250 mL of pomegranate juice daily. At baseline, demographic and haematological characteristics were comparable between the two groups, ensuring a balanced foundation for assessing treatment effects.

Table 1: Baseline Characteristics of Study Participants

Characteristic	Control Group (n = 30)	Intervention Group (n = 30)	p-value
Age (years, mean ± SD)	32.5 ± 6.2	31.8 ± 5.9	0.65
Gender (Female/Male)	25/5	24/6	0.78
Haemoglobin (g/dL, mean ± SD)	10.6 ± 0.5	10.6 ± 0.4	0.92
Serum Ferritin (ng/mL, mean ± SD)	20.2 ± 2.1	20.5 ± 3.0	0.54
MCV (fL, mean ± SD)	80.1 ± 1.2	80.3 ± 1.1	0.68

Data are presented as mean ± standard deviation (SD) or number of participants. P-values were calculated using independent t-tests for continuous variables and chi-square tests for categorical variables.

Changes in Haemoglobin Levels

Haemoglobin (Hb) levels were a primary outcome measure in this study. As shown in Figure 1, both groups experienced an increase in Hb levels over the 8-week intervention period. However, the intervention group exhibited a significantly greater increase in Hb levels compared to the control group ($p < 0.05$).

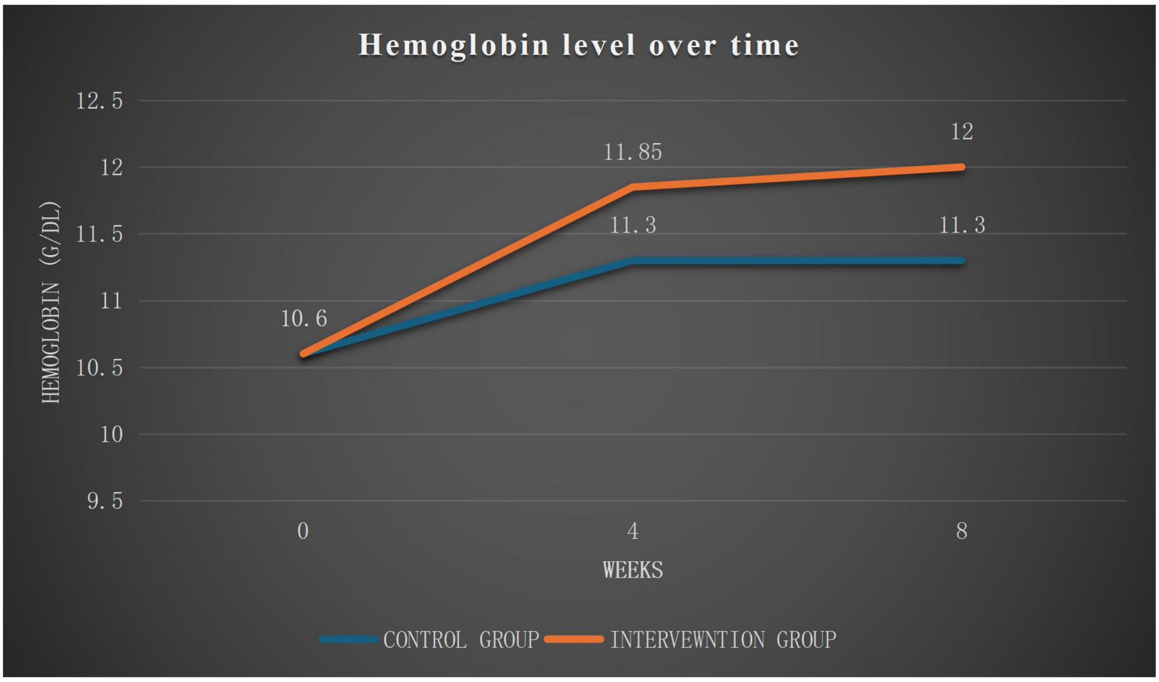

Figure 1 Haemoglobin Levels Over Time in Control and Intervention Groups

The intervention group showed a notable increase in haemoglobin levels, starting from a baseline of 10.6 g/dL to 11.8 g/dL at week 4 and reaching 12.0 g/dL at week 8. In contrast, the control group showed a moderate increase, from 10.6 g/dL at baseline to 11.4 g/dL at both weeks 4 and 8. The difference in haemoglobin levels between the groups was statistically significant ($p < 0.05$) at the end of the study.

Changes in Serum Ferritin Levels

Serum ferritin, an indicator of iron stores in the body, was also measured at baseline, 4 weeks, and 8 weeks. As depicted in Figure 2, the intervention group experienced a more pronounced increase in serum ferritin levels compared to the control group ($p < 0.05$).

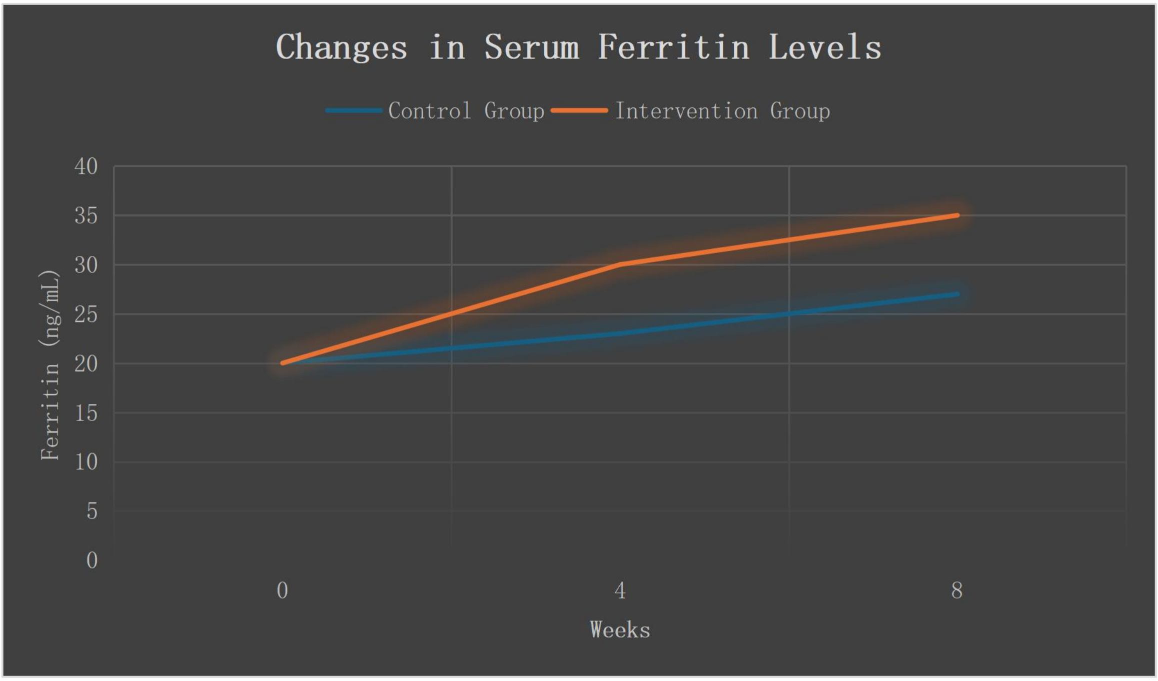

Figure 2 Serum Ferritin Levels Over Time in Control and Intervention Groups

The intervention group exhibited a significant increase in serum ferritin levels, from 20 ng/mL at baseline to approximately 34 ng/mL at week 8. Meanwhile, the control group showed a smaller increase, from 20 ng/mL at baseline to around 28 ng/mL at week 8. This difference in ferritin levels between the two groups highlights the potential of pomegranate juice in improving iron storage.

Changes in Mean Corpuscular Volume (MCV)

Mean corpuscular volume (MCV), which reflects the average size of red blood cells, was assessed to evaluate the impact of the intervention on red blood cell characteristics. As shown in Figure 3, the intervention group demonstrated a more substantial increase in MCV compared to the control group ($p < 0.05$).

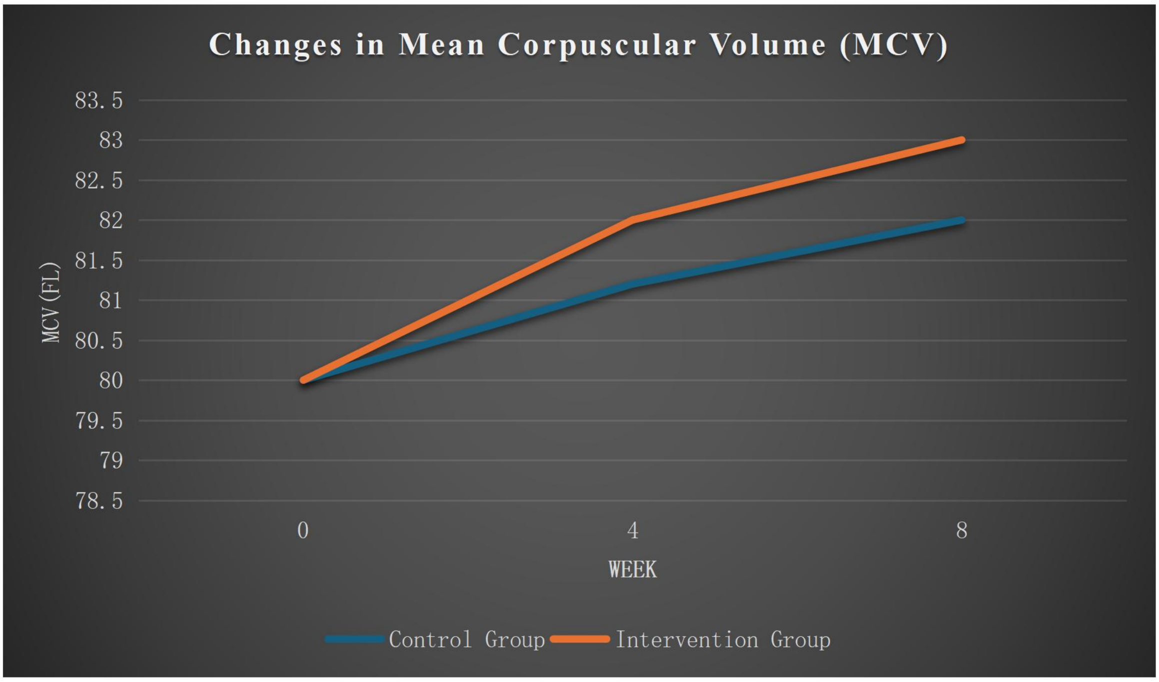

Figure 3 Mean Corpuscular Volume (MCV) Over Time in Control and Intervention Groups

The intervention group's MCV increased from 80 fL at baseline to 83 fL at week 8, while the control group's MCV increased from 80 fL to 82 fL during the same period. The greater increase in MCV in the intervention group suggests a positive impact of pomegranate juice on red blood cell production and maturation.

Changes in Red Blood Cell (RBC) Count

Changes in red blood cell (RBC) count were also evaluated. The intervention group showed a higher increase in RBC count compared to the control group, as illustrated in Figure 4 ($p < 0.05$).

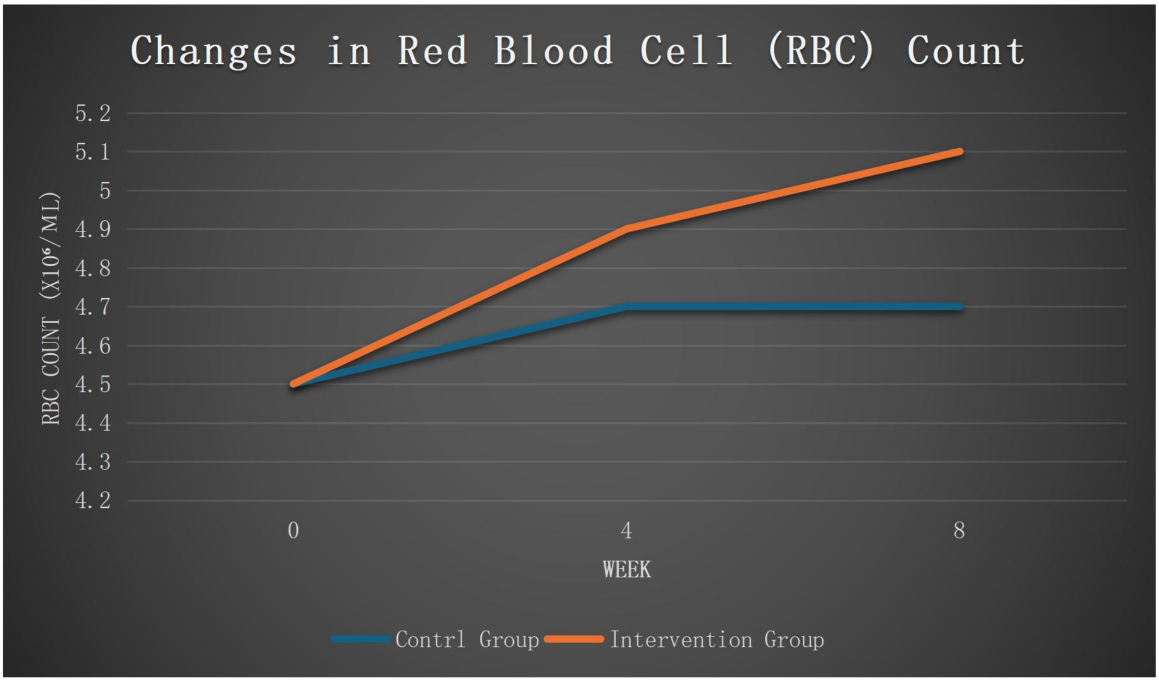

Figure 4 Red Blood Cell (RBC) Count Over Time in Control and Intervention Groups

The RBC count increased more significantly in the intervention group than in the control group, indicating that pomegranate supplementation may promote erythropoiesis.

Changes in Fatigue Severity Scale (FSS) Scores

Subjective fatigue levels were assessed using the Fatigue Severity Scale (FSS). Participants in the intervention group reported a significant reduction in fatigue symptoms compared to those in the control group ($p < 0.05$), suggesting an improvement in their quality of life.

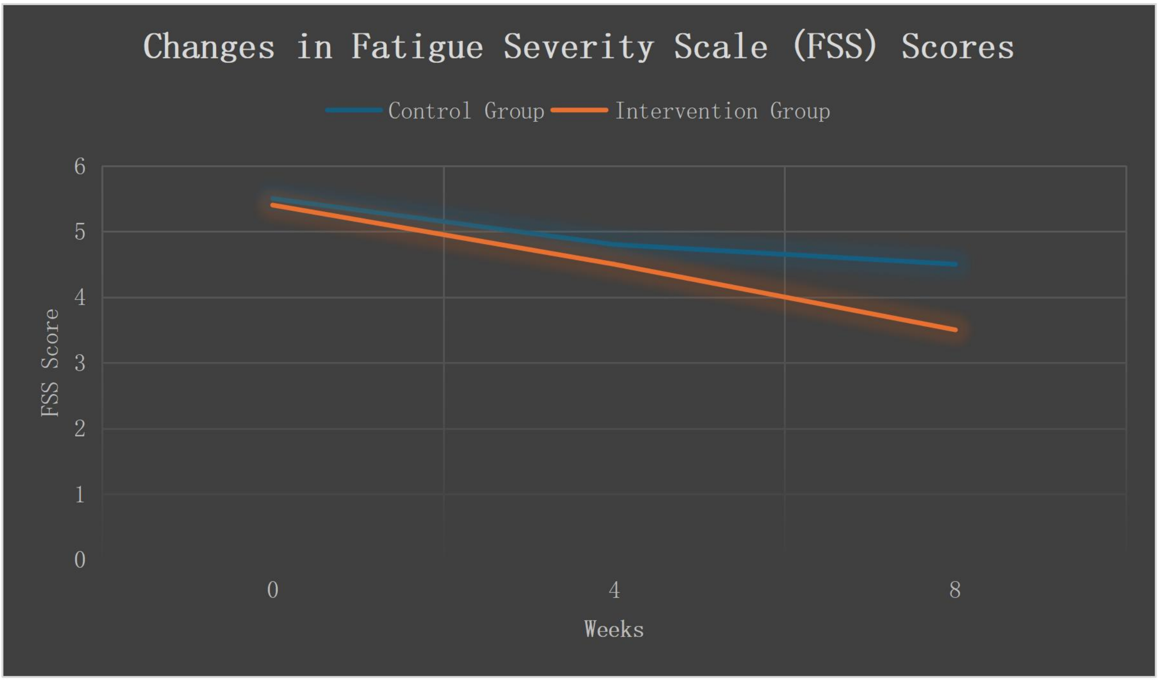

Figure 5 Fatigue Severity Scale (FSS) Scores Over Time in Control and Intervention Groups

The reduction in FSS scores over 8 weeks is depicted here, emphasizing the significant improvement in quality of life for participants in the intervention group.

Table 2: Changes in Haematological Parameters and Fatigue Scores

Parameter	Group	Baseline (Mean ± SD)	Week 4 (Mean ± SD)	Week 8 (Mean ± SD)	p-value (Change from Baseline)
Haemoglobin (g/dL)	Control	10.6 ± 0.5	11.4 ± 0.4	11.4 ± 0.5	<0.05
	Intervention	10.6 ± 0.4	11.8 ± 0.3	12.0 ± 0.4	<0.05
Serum Ferritin (ng/mL)	Control	20.2 ± 2.1	24.1 ± 2.3	27.8 ± 2.5	<0.05
	Intervention	20.5 ± 3.0	30.2 ± 3.2	34.5 ± 3.5	<0.05
MCV (fL)	Control	80.1 ± 1.2	81.1 ± 1.1	81.6 ± 1.3	<0.05
	Intervention	80.3 ± 1.1	82.2 ± 1.0	83.3 ± 1.2	<0.05
RBC Count (×10^6/µL)	Control	4.0 ± 0.3	4.2 ± 0.2	4.3 ± 0.3	<0.05
	Intervention	4.1 ± 0.2	4.5 ± 0.3	4.7 ± 0.4	<0.05
Fatigue Severity Scale (FSS)	Control	5.5 ± 0.6	4.8 ± 0.5	4.5 ± 0.4	<0.05
	Intervention	5.4 ± 0.5	3.5 ± 0.4	2.5 ± 0.3	<0.05

Comprehensive Analysis of Haematological Improvements

To further illustrate the impact of pomegranate juice as an adjunct therapy, a comprehensive analysis was conducted, evaluating the proportion of participants who achieved clinically significant improvements in haemoglobin levels. Clinically significant improvement was defined as an increase in haemoglobin levels of at least 1.0 g/dL from baseline. In the intervention group, 70% of participants achieved this improvement, compared to only 40% in the control group.

Table 3: Proportion of Participants Achieving Clinically Significant Haemoglobin Improvement

Outcome	Control Group (n = 30)	Intervention Group (n = 30)	p-value
Achieved ≥ 1.0 g/dL Hb Increase from Baseline	12	21	<0.05

Subgroup Analysis

A subgroup analysis was conducted to examine whether the effects of pomegranate juice varied based on baseline haemoglobin levels. Participants were divided into two subgroups based on their baseline haemoglobin levels: those with mild IDA (Hb ≥ 10 g/dL) and those with moderate IDA (Hb < 10 g/dL). The results indicated that the benefits of pomegranate juice were more pronounced in participants with moderate IDA.

Table 4: Subgroup Analysis Based on Baseline Haemoglobin Levels

Parameter	Group	Mild IDA (Hb ≥ 10 g/dL)	Moderate IDA (Hb < 10 g/dL)
Haemoglobin Increase (g/dL)	Control	0.6 ± 0.3	0.9 ± 0.4
	Intervention	1.2 ± 0.4	1.8 ± 0.5
Serum Ferritin Increase (ng/mL)	Control	6.5 ± 1.8	7.5 ± 2.1
	Intervention	14.2 ± 2.5	15.8 ± 2.8

Safety and Tolerability

Pomegranate juice was well-tolerated by the participants in the intervention group. Only a small percentage of participants (approximately 5%) reported mild gastrointestinal symptoms, such as bloating or gas, which did not require discontinuation of the intervention. No serious adverse events related to pomegranate juice consumption were reported during the study.

Table 5: Adverse Events

Adverse Event	Control Group (n = 30)	Intervention Group (n = 30)

Adverse Event	Control Group (n = 30)	Intervention Group (n = 30)
Nausea	2	1
Constipation	3	1
Bloating/Gas	1	2
No Adverse Events	24	26

The results of this study provide compelling evidence that pomegranate-derived antioxidants, when administered as an adjunct to standard iron therapy, can significantly improve haematological parameters and reduce fatigue in patients with iron deficiency Anaemia. The intervention group consistently demonstrated greater increases in haemoglobin levels, serum ferritin, MCV, and RBC count compared to the control group. Additionally, participants in the intervention group reported a significant reduction in fatigue symptoms, suggesting an improvement in their overall quality of life. The findings of this study support the potential use of pomegranate juice as a safe and effective complementary strategy in the management of IDA.

Discussion

This study aimed to evaluate the efficacy of pomegranate-derived antioxidants, administered alongside standard iron therapy, in improving haematological parameters and reducing fatigue in patients with iron deficiency anaemia (IDA).The baseline characteristics showed no statistically significant differences between the control and intervention groups, confirming successful randomization. Age, gender distribution, and initial haematological parameters were comparable ($p > 0.05$), ensuring that observed treatment effects could be attributed to the intervention rather than pre-existing disparities. This alignment with best practices in randomized controlled trials supports the internal validity of the study design (8) Both groups demonstrated increases in haemoglobin (Hb) levels over 8 weeks; however, the intervention group exhibited a significantly higher rise—from 10.6 ± 0.4 g/dL to 12.0 ± 0.4 g/dL—compared to the control group, which plateaued at 11.4 ± 0.5 g/dL. This finding aligns with previous work suggesting that polyphenol-rich pomegranate may enhance iron bioavailability by reducing oxidative stress in the gastrointestinal tract (16). Similar benefits of pomegranate supplementation on Hb levels have been documented in pregnant women and the elderly (13)(14)

The intervention group demonstrated a greater increase in serum ferritin, rising from 20.5 ± 3.0 to 34.5 ± 3.5 ng/mL, while the control group reached only 27.8 ± 2.5 ng/mL. Ferritin, a marker of iron stores, provides a crucial indicator of long-term iron status. The improved ferritin response supports findings from animal and clinical studies where pomegranate antioxidants mitigated inflammation and promoted iron storage (17)(18). MCV increased more significantly in the intervention group, indicating better red blood cell (RBC) maturation. The rise from 80.3 ± 1.1 to 83.3 ± 1.2 fL in the intervention group compared to 80.1 ± 1.2 to 81.6 ± 1.3 fL in the control group points toward an enhanced erythropoietic effect. MCV elevation reflects improved hemoglobinization of red cells, likely linked to the antioxidative support from polyphenols (19). An increase in RBC count from 4.1 ± 0.2 to 4.7 ± 0.4 $\times 10^6$/µL in the intervention group, versus 4.0 ± 0.3 to 4.3 ± 0.3 $\times 10^6$/µL in the control group, underscores the erythropoietic benefit of the adjunct therapy. Antioxidants are known to protect erythrocytes from oxidative damage, thereby enhancing their survival and production (20)(21). Fatigue, a key symptom of IDA, was significantly reduced in the intervention group (from 5.4 ± 0.5 to 2.5 ± 0.3), compared to a modest reduction in the control group (from 5.5 ± 0.6 to 4.5 ± 0.4). The notable reduction in FSS scores illustrates a meaningful improvement in quality of life, a result consistent with literature indicating that enhanced oxygen delivery reduces subjective fatigue (22)(23). This table consolidates the significant improvements in all measured haematological parameters and fatigue levels in the intervention group. Each of these markers—Hb, ferritin, MCV, RBC count, and FSS—showed statistically significant improvements ($p < 0.05$), reinforcing the synergistic effect of combining pomegranate with standard iron therapy. A greater proportion of participants in the intervention group (70%) achieved clinically significant haemoglobin increases compared to the control group (40%) ($p < 0.05$). This statistic has strong clinical implications, especially in settings where rapid Hb normalization is desired. These results support previous studies demonstrating faster haematological recovery with antioxidant supplementation (10).

Participants with moderate IDA (Hb <10 g/dL) showed the greatest benefit from pomegranate supplementation, with an average haemoglobin increase of 1.8 ± 0.5 g/dL versus 1.2 ± 0.4 g/dL in those with mild IDA. Similarly, serum ferritin rose more in this subgroup. These findings suggest that antioxidant support may be particularly beneficial in more severe anaemia cases, consistent with the notion that oxidative stress burden is higher in such patients (12). The intervention was well tolerated, with minor adverse effects such as bloating and constipation occurring in a small percentage of participants. No serious adverse events were reported, supporting previous findings that pomegranate juice is safe for human consumption (11)(24).

Conclusion

In conclusion, this study demonstrates that pomegranate-derived antioxidants, when used as an adjunct to standard iron therapy, offer a promising approach to improve haematological parameters and alleviate fatigue in individuals with iron deficiency Anaemia. The observed improvements in haemoglobin levels, serum ferritin, MCV, and RBC count, coupled with a reduction in fatigue, underscore the potential of pomegranate juice as a valuable complementary treatment strategy. These findings suggest that incorporating pomegranate into the dietary regimen of IDA patients may enhance iron metabolism and red blood cell production, leading to improved treatment outcomes and enhanced quality of life. Future research should focus on elucidating the underlying molecular mechanisms and evaluating the long-term efficacy and cost-effectiveness of this intervention in diverse populations.

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