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# The Effect of Ramadan Fasting Alone or in Conjunction with Physical Activity on Hematological Factors and Insulin Resistance in Adult Muslims: A Systematic Review and Meta-Analysis

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FBG: Fasting blood glucose
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Plt: Platelets

A B S T R A C T

This systematic review and meta-analysis aimed to evaluate the effects of Ramadan fasting, either alone or combined with physical exercise, on blood hematological factors and insulin resistance in adult Muslims. Six electronic databases (Web of Science, Embase (Ovid), Cochrane Library, PubMed/Medline, and Scopus) and Google Scholar were searched to identify relevant studies. We employed random-effects models to estimate the weighted mean difference (WMD) with 95% confidence intervals (CIs). The limitations of this study include the following: only English-language articles were considered, and there was variability in the types of fasting observed during Ramadan, measurement conditions, fasting duration, and ambient temperature. A total of twenty-three studies were included in the analysis. The meta-analysis indicated that fasting combined with exercise reduced HOMA-IR and white blood cell count. While no significant differences were observed between the fasting-only group and the fasting-plus-exercise group regarding insulin levels, fasting blood glucose, red blood cell count, hemoglobin, hematocrit, and platelet count, the group that combined fasting with exercise demonstrated a more favorable effect on these variables compared to the fasting-only group. Our findings suggest that fasting combined with exercise reduced HOMA-IR and white blood cell count in adult Muslims. Furthermore, this combined approach did not alter insulin, fasting blood glucose, red blood cells, hemoglobin, hematocrit, or platelet levels. Regular physical activity during Ramadan can shed light on the impact of fasting on metabolic health. Consistent physical activity combined with a balanced diet appears to be an effective strategy for improving insulin resistance and hematological indices during Ramadan. This approach has the potential to enhance metabolic health and overall well-being.

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## Introduction

The month of Ramadan is the most significant lunar month for Muslims worldwide, characterized by restrictions on eating, drinking, and the use of tobacco products [1]. This month, with its distinctive characteristics, induces changes in dietary habits, energy intake, sleep patterns, and daily physical activities, which may lead to various physiological alterations [2, 3]. According to existing evidence, fasting can be defined in multiple ways. One of these definitions is the traditional fasting observed during Ramadan (Ramadan fasting, RF), which involves abstinence from food and drink for varying periods, typically 12 hours or more. It is also considered a time-restricted feeding, with or without caloric restriction. In this context, intermittent fasting (IF) encompasses several subcategories, including alternate-day fasting (ADF), intermittent energy restriction (IER), time-restricted feeding (TRF), and traditional Ramadan fasting [4, 5].

Intermittent fasting (IF) encompasses various approaches characterized by prolonged fasting intervals and designated periods for food consumption, which may or may not involve caloric restriction. The three most widely recognized methods include the 5:2 diet,

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alternate-day fasting (ADF), and time-restricted feeding (TRF) [6]. In the 5:2 diet, participants limit their caloric intake to 400–600 kcal on two non-consecutive days each week while eating unrestrictedly on the remaining days. The ADF method alternates between 24-hour fasting and subsequent 24-hour periods where individuals can eat freely. This approach can be modified to allow the consumption of up to 25% of daily caloric needs on fasting days, referred to as modified alternate-day fasting (MADF) [7, 8]. Among these, TRF is the most extensively studied, focusing on constraining the daily eating window [9]. Participants are instructed to consume all meals within a designated time frame, such as 8 to 10 hours, and to refrain from consuming any energy-containing foods or beverages during the remaining 14 to 16 hours of the day [10].

Regardless of the specific fasting protocol, prolonged periods of reduced or absent nutrient intake inherently characterize all fasting modalities. A potential consequence of such energy restriction is the catabolism of lean body mass (LBM). Skeletal muscle mass, a key component of LBM, is particularly vulnerable, with its maintenance depending on the dynamic balance between protein synthesis and degradation [11]. Consequently, intermittent fasting strategies may negatively impact human health and athletic performance, including psychological factors such as motivation, physiological processes like muscle recruitment, and biochemical parameters such as plasma volume and glycogen stores [12-14]. Conversely, some studies have reported beneficial effects, such as reduced circulating cholesterol and triglyceride concentrations, in specific fasting contexts, such as Ramadan. Research has demonstrated that fasting during Ramadan can lower LDL-C (low-density lipoprotein cholesterol, commonly referred to as "bad cholesterol") and triglycerides (TG), contributing to improvements in blood lipid profiles [15, 16]. Reducing caloric intake during fasting may alter hormone levels, promote the breakdown and metabolism of stored fats, and lead to more significant fat loss than other calorie-restriction methods. Moreover, consistent fasting may increase muscle mass and reduce body fat [17]. Insulin resistance is another significant factor that fasting can influence. Fasting leads to a reduction in blood insulin levels and significantly enhances insulin sensitivity, a benefit particularly evident in obese and diabetic individuals, as it may reduce the risk of developing type 2 diabetes [18]. Among the mechanisms associated with the effects of fasting and physical activity on insulin sensitivity, it is noted that these two interventions directly increase glucose uptake by muscles, meaning that muscles absorb more glucose from the bloodstream. This effect is facilitated by increased glucose transporters (GLUT4) in muscles during physical exercise. Regular physical activity can thus enhance glucose transport and improve lipid metabolism, ultimately strengthening insulin sensitivity [19]. Evidence suggests that fasting during Ramadan and engaging in physical activities lead to significant changes in insulin resistance indices [20, 21], hematological parameters [22, 23], and body composition [24]. Elmajnounw et al. [18] conducted a systematic review and meta-analysis to investigate the effects of Ramadan fasting (RF) on blood glucose control. The study reviewed 1,592 articles and analyzed 12 studies comprising 5,554 participants (54% male and 46% female). The findings revealed a significant reduction in HbA1c levels (WMD = 0.55 mg/dl, $P < 0.00001$) and fasting blood glucose (FBG) levels (WMD = 12.42, $P < 0.0001$) after RF intervention compared to pre-fasting measurements. However, no significant change in body weight was observed among individuals who fasted during Ramadan. Yang et al. [25] performed a systematic review to investigate the impact of intermittent fasting (IF) on cardiometabolic risk factors (CMRFs). The review included 14 randomized controlled trials comparing IF interventions with control group diets. The results indicated that participants who followed IF interventions exhibited significant reductions in various health metrics compared to the control groups. Specifically, reductions were observed in body weight (WMD, -1.78 kg; $p < 0.05$), waist circumference (WMD, -1.19 cm; $p < 0.05$), fat mass (WMD, -1.26 kg; $p < 0.05$), and body mass index (WMD, -0.58 kg/m$^2$; $p < 0.05$). Additionally, there were reductions in systolic blood pressure (WMD, -2.14 mmHg; $p < 0.05$), diastolic blood pressure (WMD, -1.38 mmHg; $p < 0.05$), fasting blood glucose (WMD, -0.053 mmol/L; $p < 0.05$), fasting insulin (WMD, -0.8 mIU/L; $p < 0.05$), and insulin resistance (WMD, -0.21; $p < 0.05$). These findings suggest that the IF approach is associated with more favorable metabolic profiles, likely contributing to positive changes in insulin resistance and athletic performance. However, there is limited information regarding the effects of different IF protocols on markers of insulin resistance and hematological parameters. While most studies have focused on the impact of restricted feeding windows, with or without caloric restriction, time-restricted feeding (TRF), or fasting for several days or weeks on lipid profile factors [26, 27] and liver enzymes [28], no study has yet investigated the combined effects of exercise interventions and intermittent fasting on hematological parameters and insulin resistance markers. Moreover, it remains unclear whether the physiological outcomes observed can be solely attributed to intermittent fasting itself or to the combined effects of exercise interventions alongside intermittent fasting.

The criteria for including studies in this systematic review were as follows: participants must be Muslims who observe fasting during Ramadan, regardless of age or gender, and must be adults aged 18 years or older who underwent testing during Ramadan. Additionally, participants should not have experienced any injuries. The interventions considered included Ramadan diurnal intermittent fasting and alternate-day fasting, with the condition that participants had not engaged in any exercise training six months before the study. Furthermore, a comparison was made between individuals in the fasting plus exercise group and those in the fasting-only group. This systematic review aims to investigate whether there is a difference between the effects of intermittent fasting alone and the combined effects of various exercise interventions with intermittent fasting on hematological parameters and markers of insulin resistance in fasting individuals.

## Materials and Methods

### *Search Strategy*

A comprehensive search was conducted across six electronic databases: Web of Science, Embase (Ovid), Cochrane Library, PubMed/Medline, Scopus, and Google Scholar, with no temporal limitations applied. This search aimed to identify all relevant studies, including systematic reviews and meta-analyses, and involved manually reviewing the reference lists of selected articles to identify additional eligible studies. The search strategy was specifically designed to identify randomized controlled trials (RCTs) that examined the effects of physical activity and fasting or compared the effects of these two interventions on health-related outcomes. The strategy followed a population, intervention, and outcome framework, using a combination of medical subject headings and free-text terms based on relevant keywords. "intermittent fasting" or "Ramadan fasting" or "Ramadan" or "fasting" or "Ramadan intermittent fasting", or "religious fasting", or "IF", or "time restricted feeding", or "TRF", or "modified alternate day fasting", or "ADF", or "MADF", or " alternate day calorie restriction", or " time-restricted feeding", or " alternate day fasting", or "red blood cell", or "white blood cells", or "hematocrit", or "hemoglobin", or "platelet", or "fasting blood glucose", or "insulin", or "HOMA-IR", or "strength training", or "physical activity", or "combined training", or "exercise training", or "aerobic training", or "anaerobic training", or "resistance training", or "circuit training", or "circuit weight training", or "interval training", or "chronic training" or "Yoga". Boolean search operators (AND, OR, NOT) combined search terms related to exercise training participation with outcomes associated with Ramadan fasting. The search terms included "Ramadan," "fasting," "Ramadan intermittent fasting," "alternate-day calorie restriction," "time-restricted feeding," "alternate-day fasting," and "religious fasting." Duplicate publications were identified by comparing author names, treatment comparisons, publication dates, sample sizes, interventions, and outcomes. Based on a search conducted across multiple databases, the researcher included studies published between 1999 and 2021. The final search for articles continued until November 23, 2024. Two authors independently reviewed article titles, assessed abstracts, and selected relevant studies for inclusion in the manuscript. They followed a four-step process outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, including identification, screening, eligibility, and inclusion, to narrow the initial search results. The current study adhered to the PRISMA guidelines [29].

### *Selection Criteria*

The criteria for study inclusion were based on the Participants, Intervention, Comparison, Outcome, and Study design (PICOS) framework.

To assess article eligibility, two authors (KH and AT) independently reviewed the relevant articles' titles, abstracts, and full texts. Studies were considered eligible if they met the following requirements: (1) Population: Muslims who observe Ramadan fasting, regardless of age or sex, with samples of adults (aged ≥ 18 years) who underwent testing during the month of Ramadan; participants should not have experienced any injuries; (2) Intervention: Ramadan diurnal intermittent fasting, alternate-day fasting, in which participants did not engage in exercise training within the six months before the study; (3) Comparison: Fasting plus exercise group versus fasting-only (non-exercise) group; (4) Outcomes: Red blood cells ($10^3$/μL), white blood cells ($10^3$/μL), hematocrit (%), hemoglobin (g/dL), platelets ($10^3$/μL), fasting blood glucose (mg/dL), insulin (mIU/mL), and HOMA-IR; (5) Study Design: Randomized controlled trials (RCTs) published in English.

### Data Extraction

The screening of publications identified through the search was conducted independently by two authors, KH and AT, using predefined inclusion and exclusion criteria in cases of disagreement regarding the inclusion of ambiguous articles. A third author, MRM, served as an adjudicator. The extracted data included publication details (e.g., first author's name, publication year, country, duration of daytime fasting, temperature, and relative humidity), study specifics (e.g., sample sizes for both intervention and control groups, health status, and exercise model), participant characteristics (e.g., BMI and average age), and a description of the intervention (including exercise type, duration, frequency, intensity, sets, and repetitions). Additionally, the mean and standard deviation (SD) of hematological parameters and insulin resistance markers were recorded at baseline, post-intervention, and/or the changes observed between these two time points.

### Data Synthesis

The outcome effect size was determined by calculating the mean difference (MD) between the exercise intervention and the control condition, using pre- and post-intervention data from all included studies. Due to the consistency in reporting methods for outcomes, the MD was presented alongside a 95% confidence interval (CI). All analyses were conducted using Review Manager 5.3, developed by The Nordic Cochrane Centre in Copenhagen, Denmark. The extracted outcome data were further processed by calculating the change in mean and standard deviation (SD) values. Specifically, the baseline mean was subtracted from the post-intervention mean, and the change in SD was calculated using the number of participants in each study group, along with the corresponding group p-values or 95% CI, when the change in mean and SD was not explicitly reported. In studies that reported standard error of the mean (SEM) data instead of SD, the SEM value was converted to SD. The Standard Error of the Mean (SEM) is calculated by dividing the Standard Deviation (SD) by the square root of the sample size (N). This relationship is essential for interpreting published research findings. If the SEM is available and you wish to obtain the SD, it can be calculated by multiplying the SEM by the square root of N [30].

In cases where data were unavailable in the text or tables and the authors could not be contacted, data from figures were extracted, when possible, using GetData Graph Digitizer software. For articles that included a control group alongside multiple exercise groups, each exercise group was labeled individually, and the sample size of the control group was divided by the number of exercise groups.

To synthesize the existing research on the influence of exercise, we employed a random-effects model to derive pooled estimates for various outcome measures. Heterogeneity among the included studies was assessed using the $I^2$ statistic, with values greater than 50% considered indicative of substantial variability. Subgroup analyses were then performed to explore potential sources contributing to this observed heterogeneity [30]. Forest plots were used to represent the meta-analysis visually, and statistical significance was set at a threshold of $p < 0.05$. Additionally, funnel plots were employed to assess the potential for publication bias, with p-values below 0.05 suggesting significant bias within the dataset [31].

### Study Quality

To rigorously evaluate the methodological quality of the included studies, each investigation was independently assessed using the Tool for the Assessment of Study Quality and Reporting in Exercise (TESTEX), a fifteen-point scale specifically designed for exercise-related research. This validated instrument allows for a precise evaluation of research quality (with a minimum score of 5) and reporting completeness (with a maximum score of 10), tailored to Ramadan fasting studies [32]KH and AT conducted dual, independent assessments, and any discrepancies were resolved through discussion and consensus with MRM.

## Results

### *Study Selection*

The initial search yielded 2,194 records. After eliminating duplicates and conducting a title and abstract screening, 275 studies were selected for a comprehensive review based on predefined inclusion and exclusion criteria. Of these, 23 studies met the inclusion criteria, while 252 were excluded for various reasons: (A) Not related to the intervention of interest (n=4), (B) Not related to the outcome of interest (n=8), (C) Participants under 18 years of age (n=14), (D) Conference presentations or posters (n=8), (E) Lack of direct measurement of hematological-biochemical parameters (n=9), (F) Absence of control groups (n=140), (G) Non-English language publications (n=29), and (H) Review articles (n=40). Ultimately, 23 randomized controlled trials (RCTs) [20, 22, 24, 33-52] Eight hundred fourteen participants were included in the analysis—431 in the fasting and exercise groups and 383 in the fasting-only group. Figure 1 shows a flow diagram illustrating the study search and selection process, including reasons for exclusion.

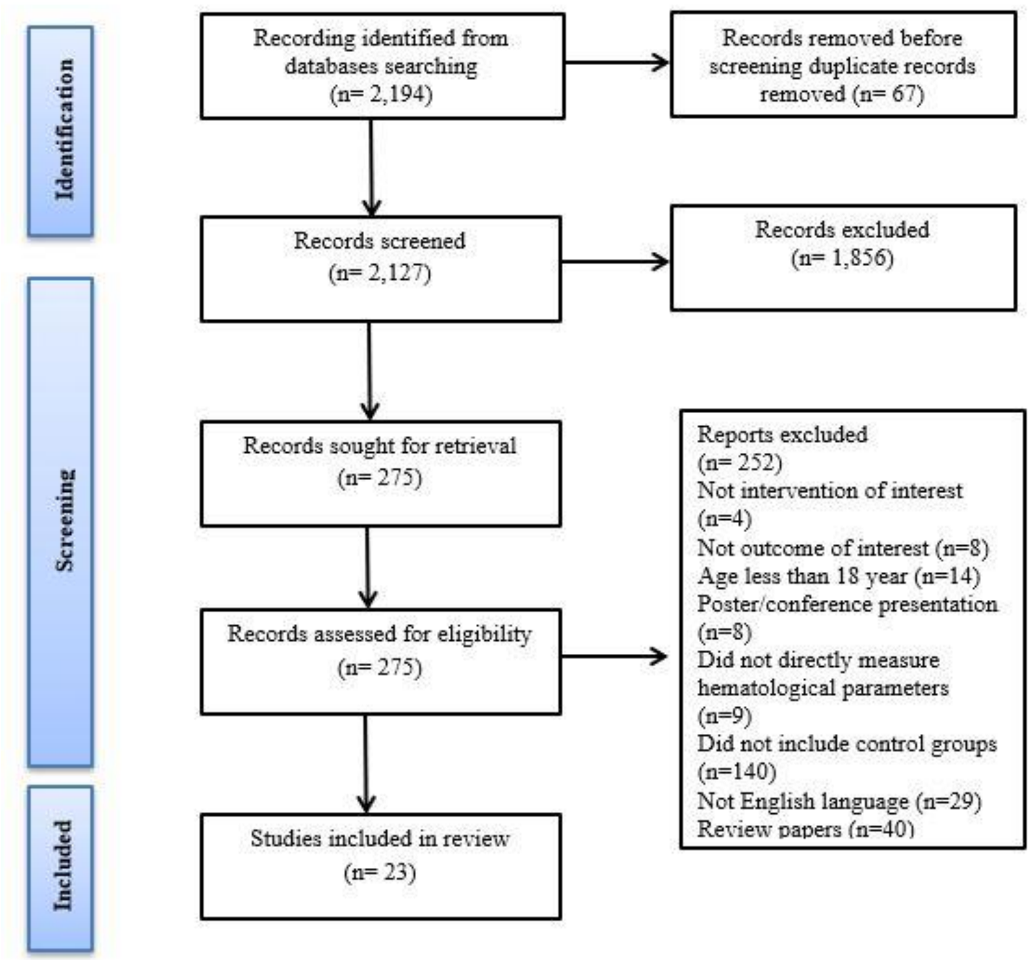


**Figure. 1.** The Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) flow chart of the systematic literate research.

### Characteristics of the Selected Studies

Studies were carried out in Iraq (1), Iran (9), Egypt (1), the USA (1), the Republic of Korea (2), the UK (3), Italy (1), Kuwait (1), Singapore (1), and Tunisia (3).

According to the criteria for biological sex classification, 13 studies focused solely on male participants [24, 33, 39-43, 45, 46, 48-51], while three studies exclusively involved female participants [34, 35, 52]. Additionally, seven studies included both male and female participants [20, 22, 36, 38, 44, 47, 53]. In terms of age, the mean age of participants across the 23 studies ranged from 18 to 44 years. Five studies did not report the mean BMI of their participants [33, 40, 43, 48, 49]. Among the studies that included adults with diabetes, five classified participants as having a normal weight based on BMI [39, 42, 46, 47, 54], seven categorized them as overweight [24, 38, 45, 50-53], and six studies included individuals classified as obese [20, 34-36, 41, 44].

### Intervention Characteristics

The duration of interventions in the studies analyzed ranged from 8 to 52 weeks, with exercise training sessions lasting between 30 and 90 minutes. The frequency of training sessions per week varied from 3 to 8. Regarding fasting duration during Ramadan, 15 studies did not specify the fasting length. In comparison, three studies reported 15 hours, one noted 16 hours, 3 indicated 12 hours, and one mentioned a range of 11 to 14 hours.

Based on the training program classification criteria, 15 studies employed aerobic exercise training [20, 22, 33-36, 38-42, 45, 46, 50, 53], six studies included resistance training [24, 43, 44, 48, 49, 51]One study included yoga training [52], and one study examined the Wingate anaerobic cycle test [47]. The relevant characteristics for each of the included studies are provided in Table S1.

### Meta-analysis Results

### Pooled Estimates of Blood Hematological and Insulin Resistance

### Hemoglobin

In general, fasting combined with exercise training and fasting alone did not significantly alter hemoglobin levels (WMD: -0.12 g/dL [95% CI, -0.85 to 0.62], p = 0.75). There was low heterogeneity ($I^2$ = 66%; p < 0.007) among the studies included in this comparison (see Figure S1 in supplementary file).

Subgroup analyses based on BMI status showed that individuals with a BMI < 25 kg/m$^2$ who participated in both fasting and exercise exhibited a significant reduction in hemoglobin levels (No. of arms: 3, WMD: -0.81 g/dL [95% CI, -1.46 to -0.16], p = 0.0001; $I^2$ = 21%, p (heterogeneity) < 0.28) compared to those in the fasting-only group. In contrast, participants with BMIs of 25.0–29.9 kg/m$^2$ and ≥ 30 kg/m$^2$ did not show statistically significant changes in hemoglobin levels.

In terms of biological sex, it was observed that men exhibited an increase in hemoglobin levels following a regimen of fasting combined with exercise training (WMD: 0.88 g/dL [95% CI, 0.17 to 1.59], p = 0.0001; $I^2$ = 0%, p (heterogeneity) < 0.80). Conversely, when both men and women were analyzed together, hemoglobin levels showed a reduction under the same fasting plus exercise training conditions (WMD: -0.65 g/dL [95% CI, -1.24 to -0.06], p = 0.0001; $I^2$ = 47%, p (heterogeneity) < 0.15), compared to the fasting-only group (see Table S2).

### Hematocrit

Generally, fasting plus exercise training and fasting did not change hematocrit (WMD: -0.29 % [95% CI, -1.31, 0.73]; p = 0.58). There was significant high heterogeneity ($I^2$=59%; p < 0.02) among studies included for this comparison (see Figure S2).

Subgroup analyses based on Body Mass Index (BMI) indicated that individuals with a BMI < 25 kg/m$^2$ (No of arms: 3, WMD: -0.76% [95% CI: -1.58 to 0.05], p = 0.07; $I^2$ = 86%, p for heterogeneity = 0.0001) and those with a BMI ≥ 30.0 kg/m$^2$ (No of arms: 2, WMD: -1.43% [95% CI: -3.73 to 0.86], p = 0.22; $I^2$ = 60%, p for heterogeneity = 0.12) did not exhibit statistically significant alterations in hematocrit levels.

Subgroup analyses based on biological sex revealed no statistically significant changes in hematocrit levels among male participants (WMD: -0.27% [95% CI, -2.05 to 1.51], p = 0.77; $I^2$ = 75%, p for heterogeneity = 0.0001). Similarly, interventions that included both male and female participants showed no significant alterations in hematocrit levels (WMD: -0.46% [95% CI, -1.45 to 0.53], p = 0.37; $I^2$ = 0%, p for heterogeneity = 0.67) (see Table S2).

***Platelet***

In general, fasting combined with exercise training and fasting alone did not significantly change platelet levels (WMD: -9.02 × $10^3$/μL [95% CI, -26.29 to 8.26], p = 0.31). There was low heterogeneity ($I^2$ = 0%; p < 0.82) among the studies included for this comparison (see Figure S3).

Subgroup analyses based on BMI categories indicated that individuals with a BMI of less than 25 kg/$m^2$ showed no statistically significant change in platelet levels (No. of arms: 2, WMD: -10.49 × $10^3$/μL [95% CI, -33.07 to 12.08], p = 0.36; $I^2$ = 0%, p for heterogeneity = 0.38). Similarly, participants with a BMI ranging from 25 to 29.9 kg/$m^2$ also exhibited no significant changes in platelet levels (No. of arms: 2, WMD: -6.31 × $10^3$/μL [95% CI, -35.43 to 22.81], p = 0.67; $I^2$ = 0%, p for heterogeneity = 0.40). These findings suggest that variations in BMI within these ranges do not significantly influence platelet count.

Subgroup analyses stratified by biological sex revealed no statistically significant changes in platelet levels among men (WMD: -6.93 × $10^3$/μL [95% CI, -33.77 to 19.91], p = 0.61; $I^2$ = 0%, p for heterogeneity < 0.70). Similarly, no significant changes were observed when analyzing combined data for both men and women (WMD: -10.49 × $10^3$/μL [95% CI, -33.07 to 12.08], p = 0.36; $I^2$ = 0%, p for heterogeneity < 0.38) (see Table S2).

***Red Blood Cell***

In general, fasting combined with exercise training and fasting alone did not significantly change red blood cell count (WMD: -0.32 × $10^3$/μL [95% CI, -0.99 to 0.36], p = 0.36). There was high heterogeneity ($I^2$ = 97%; p < 0.0001) among the studies included in this comparison (see Figure S4).

Subgroup analysis based on BMI classification indicated that individuals with a BMI of less than 25 kg/$m^2$ did not exhibit statistically significant changes in red blood cell count (No. of arms: 2, WMD: -0.53 × $10^3$/μL [95% CI, -1.58 to 0.52], p = 0.32). Notably, substantial heterogeneity was observed across studies ($I^2$ = 98%, p for heterogeneity < 0.0001).

Subgroup analyses based on biological sex revealed no statistically significant changes in red blood cell count for males (WMD: 0.11 × $10^3$/μL [95% CI, -0.11 to 0.33], p = 0.32), nor for the combined group of males and females (WMD: -0.53 × $10^3$/μL [95% CI, -1.58 to 0.52], p = 0.32; $I^2$ = 98%, p for heterogeneity < 0.0001) (see Table S2).

***White Blood Cell***

The fasting plus exercise training group generally experienced a significantly greater decrease in white blood cell count (WMD: -0.77 × $10^3$/μL [95% CI, -1.51 to -0.03], p = 0.04) compared to the fasting-only group. There was low heterogeneity ($I^2$ = 0%; p < 0.45) among the studies included in this comparison (see Figure S5).

In subgroup analyses based on BMI classification, individuals with a BMI < 25 kg/$m^2$ (No. of arms: 2, WMD: -0.91 × $10^3$/μL [95% CI, -2.00 to 0.18], p = 0.10; $I^2$ = 35%, p for heterogeneity = 0.21) and those with a BMI ≥ 30 kg/$m^2$ (No. of arms: 1, WMD: -0.56 × $10^3$/μL [95% CI, -2.33 to 1.21], p = 0.053) did not exhibit statistically significant changes in white blood cell counts.

Subgroup analyses stratified by biological sex revealed no statistically significant changes in white blood cell counts among male participants (WMD: -0.56 × $10^3$/μL [95% CI, -2.33 to 1.21], p = 0.53). Similarly, when considering both male and female participants collectively, no significant changes were observed (WMD: -0.91 × $10^3$/μL [95% CI, -2.00 to 0.18], p = 0.10; $I^2$ = 35%, p for heterogeneity < 0.45) (see Table S2).

***Fasting Insulin***

In general, fasting plus exercise training and fasting alone did not significantly change fasting insulin levels (WMD: -3.53 μIU/mL [95% CI, -7.59 to 0.52], p = 0.09). There was high heterogeneity ($I^2$ = 81%; p < 0.0003) among the studies included in this comparison (see Figure S6).

Subgroup analyses based on BMI classification revealed the following findings regarding fasting insulin levels: Among individuals with a BMI < 25 kg/$m^2$, no statistically significant changes were observed (No. of arms: 1, WMD: -2.10 μIU/mL [95% CI, -9.23 to 5.03], p = 0.56). Similarly, for those with a BMI ≥ 30 kg/$m^2$, changes in fasting insulin levels were not significant (No. of arms: 2, WMD: -4.63 μIU/mL [95% CI, -10.52 to 1.26], p = 0.12; $I^2$ = 0%, p for heterogeneity = 0.58). However, in the subgroup with a BMI ranging from 25 to 29.9 kg/$m^2$, a significant reduction in fasting insulin levels was observed (No. of arms: 1, WMD: -7.08 μIU/mL [95% CI, -9.90 to -4.26], p = 0.0001). These findings highlight BMI-specific variations in fasting insulin responses, suggesting the need for further investigation into the underlying physiological mechanisms.

The subgroup analyses stratified by biological sex revealed no statistically significant changes in fasting insulin (FI) levels among male participants (WMD: -0.67 µIU/mL; 95% CI: -1.10 to -0.24; p = 0.003). Conversely, interventions that included both male and female participants demonstrated a significant reduction in FI levels (WMD: -6.11 µIU/mL; 95% CI: -8.51 to -3.72; p = 0.0001), with no observed heterogeneity ($I^2$ = 0%, p for heterogeneity < 0.53) (see Table S2).

Fasting Blood Glucose

Overall, the combination of fasting and exercise training did not significantly change fasting blood glucose levels (WMD: 0.41 mg/dL [95% CI, -0.34 to 1.16], p = 0.28). Additionally, there was considerable heterogeneity among the studies analyzed for this comparison, with an $I^2$ value of 72% (p < 0.0001) (see Figure S7).

The analysis of BMI subgroups revealed the following findings regarding fasting insulin levels: For individuals with a BMI < 25 kg/m$^2$, no statistically significant change was observed (No. of arms: 5, WMD: 0.36 mg/dL; 95% CI: -0.61 to 1.34; p = 0.47; $I^2$ = 59%, p for heterogeneity < 0.001). Similarly, in the BMI range of 25–29.9 kg/m$^2$, no significant changes were detected (No. of arms: 4, WMD: -0.09 mg/dL; 95% CI: -0.36 to 0.17; p = 0.48; $I^2$ = 0%, p for heterogeneity = 0.83). Finally, fasting insulin levels also showed no significant changes for individuals with a BMI ≥ 30 kg/m$^2$ (No. of arms: 1, WMD: -3.10 mg/dL; 95% CI: -8.14 to 1.94; p = 0.23). These findings suggest that variations in BMI do not significantly affect fasting insulin levels across these subgroups.

Subgroup analyses based on biological sex revealed that male participants showed no statistically significant changes in fasting blood glucose levels (WMD: 0.64 mg/dL [95% CI, -0.64 to 1.92], p = 0.33; $I^2$ = 78%, p for heterogeneity = 0.0001). Similarly, interventions involving both male and female participants demonstrated no significant changes in fasting blood glucose (WMD: -2.96 mg/dL [95% CI, -1.06 to 6.97], p = 0.15; $I^2$ = 72%, p for heterogeneity = 0.0001), as detailed in Table S2.

HOMA-IR

In general, the fasting plus exercise training group experienced a significantly more significant decrease in HOMA-IR (WMD: -1.65 [95% CI, -2.25 to -1.04], p = 0.0001), with low heterogeneity ($I^2$ = 0%; p < 0.70) compared to the fasting-only group (see Figure S8).

The analysis of BMI subgroups revealed the following outcomes: For individuals with a BMI < 25 kg/m$^2$, no statistically significant effect was observed (No. of arms: 1, WMD: -0.70 [95% CI, -2.66 to 1.26], p = 0.48). A significant reduction in HOMA-IR was noted in the BMI range of 25–29.9 kg/m$^2$ (No. of arms: 1, WMD: -1.80 [95% CI, -2.49 to -1.11], p = 0.001). However, for individuals with a BMI ≥ 30 kg/m$^2$, no significant changes in HOMA-IR were detected (No. of arms: 2, WMD: -1.45 [95% CI, -3.11 to 0.20], p = 0.08). The heterogeneity for this subgroup was low ($I^2$ = 0%, p for heterogeneity < 0.70), as detailed in Table S2.

***Study quality***

The methodological rigor of the analyzed studies was evaluated using the TESTEX scale, a 15-point instrument designed to assess study quality. Our analysis revealed an overall quality ranging from moderate to good, with a median TESTEX score of 9 (7–12). While several studies demonstrated high quality, with two achieving a score of 12, specific methodological weaknesses were consistently observed. Specifically, essential aspects such as explicit randomization procedures, allocation concealment, assessor blinding, intention-to-treat analyses, and physical activity monitoring within control groups were inadequately addressed in a significant proportion of the included studies. Further details on the risk of bias, as assessed using the Cochrane tool, are provided in Figure 2.

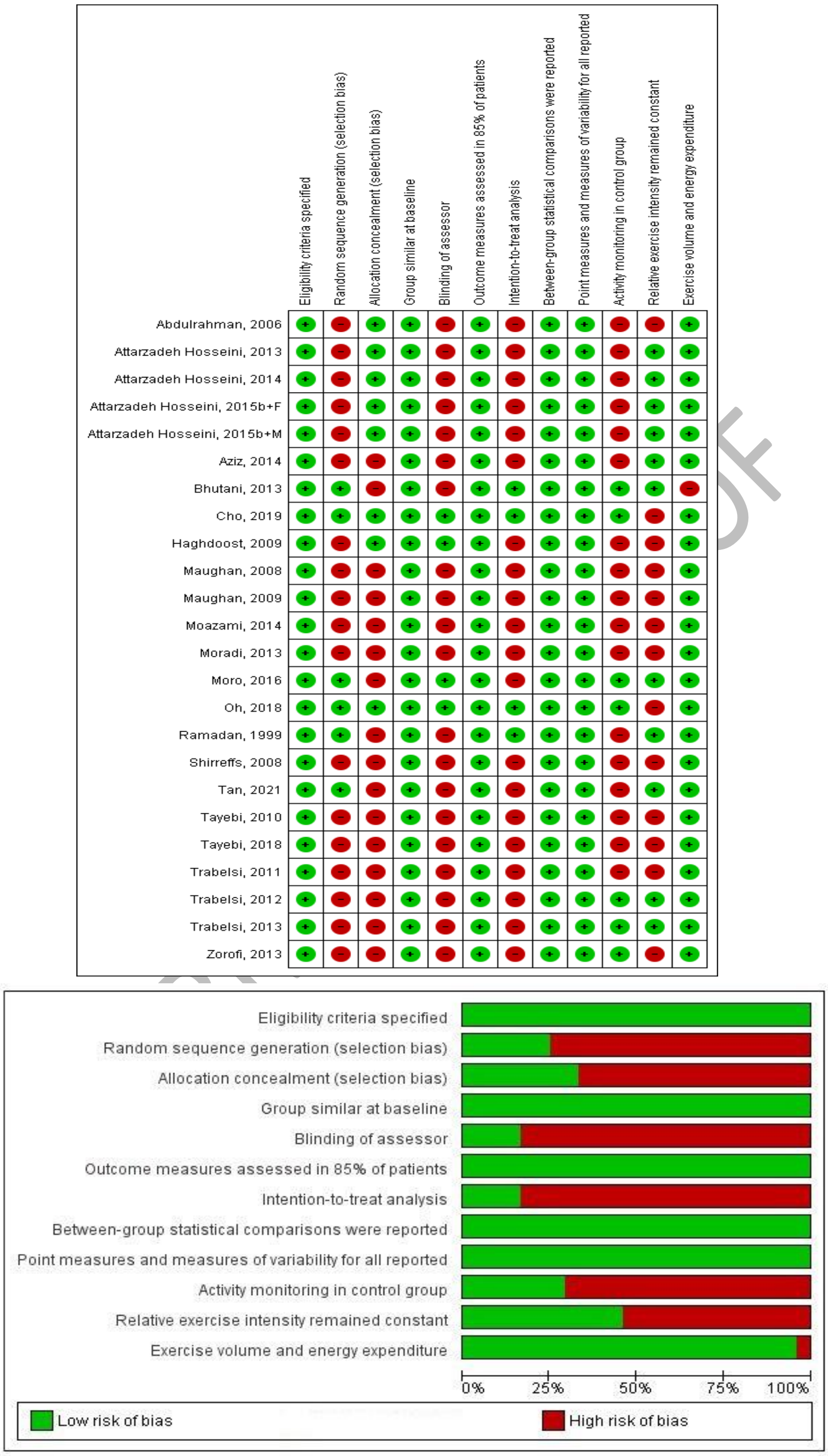


**Figure 2.** Risk of bias assessment using Cochrane risk of bias tool. Top panel—Risk of bias summary showing review author's judgment about each risk of bias item for each included study. Bottom panel—Risk of bias graph showing review author's judgment about each risk of bias item presented as percentages across all included studies.

## Discussion

This systematic review and meta-analysis were conducted to investigate the effects of Ramadan fasting, either alone or combined with physical exercise, on blood hematological factors and markers of insulin resistance in adult Muslims. The pooled results from 23 RCTs (814 participants, 431 in the fasting and exercise groups, and 383 in the fasting-only groups) showed that the fasting plus exercise training group experienced a significantly more significant decrease in white blood cell count and HOMA-IR. However, no significant changes were observed in red blood cell count, hematocrit, hemoglobin, platelet count, fasting blood glucose, or insulin levels following fasting and exercise.

Additionally, gender influenced the effectiveness of fasting plus exercise, with more significant reductions in hemoglobin levels observed in both male and combined male and female participants. Regarding fasting insulin, significant changes were observed only in the combined group (male and female), while no significant effects were noted in the male-only group. Furthermore, Body Mass Index (BMI) status influenced the efficacy of the fasting and exercise combination, with more significant decreases in hemoglobin levels seen among participants with a normal BMI. Overall, the quality of the studies in the meta-analyses ranged from moderate to good. Most analyses showed moderate to high levels of heterogeneity and evidence of publication bias.

Fasting combined with exercise training significantly reduced patients' white blood cell count (WMD: -0.77 × $10^3$/µL [95% CI, -1.51 to -0.03], p = 0.04). However, no significant differences among fasting individuals were observed in red blood cell count, hematocrit, hemoglobin, platelet count, fasting blood glucose, or insulin levels after Ramadan. The findings from this review are consistent with those of Rejeb et al. [55], who found that Ramadan fasting (RF) caused a significant reduction in white blood cell count in male Muslims. Numerous studies have reported varying results regarding changes in red blood cell (RBC) parameters. For instance, while some studies [56, 57] indicated that levels of RBC, hemoglobin (Hb), and hematocrit (Ht) remained stable, others observed either a minor degree of hemoconcentration [58] or a notable decline in Hb and Ht [59]. Additionally, several studies documented a significant decrease in platelet (Plt) counts [56, 60]. In research conducted by Sarraf-Zadegan et al. [61], it was found that mean levels of hemoglobin (Hb), hematocrit (Ht), and red blood cells (RBC) were significantly elevated in the End-R phase compared to the After-R phase. In contrast, platelet levels were reduced considerably, and white blood cell (WBC) levels remained comparable. Similarly, Al-Hourani et al. [56] (2009) concluded that the mean levels of Plt in the Mid-R phase were significantly lower compared to the Before-R phase, while Hb, Ht, and RBC levels showed no significant differences. Conversely, the study by Sedaghat et al. [62] demonstrated that, compared to the Before-R data, the After-R mean levels for hematocrit (Ht) and mean corpuscular volume (MCV) were significantly lower. In contrast, mean corpuscular hemoglobin (MCH) levels were significantly higher. Hemoglobin (Hb), red blood cell (RBC), white blood cell (WBC), and platelet (Plt) levels remained similar. Prolonged periods of starvation lead mammals to significantly reduce their energy expenditure by decreasing the size of various tissues, organs, and cellular populations, including blood cells. The subsequent restoration of these components during refeeding highlights a potential mechanism for hematopoietic regeneration and the synchronized recovery of other bodily systems and organs [63]. Extended starvation has been associated with a notable decline in white blood cell counts. A coordinated response is activated during the refeeding phase to address this immune deficiency. This results in a marked increase in hematopoietic cells that seek to restore equilibrium within the cellular population. This process effectively reestablishes balance even after significantly suppressing white blood cells [55]. Moreover, prolonged fasting cycles can restore normal white blood cell counts and re-establish lineage balance, even following severe suppression due to chemotherapy or aging. This suggests that the organism can regenerate its hematopoietic system through fasting, regardless of the underlying cause of the deficiency [64]. A decrease in red blood cell count, contributing to reduced hematocrit levels, can be linked to diminished production of red blood cells stemming from a lack of red blood cell precursors [65]. In this investigation, a reduction in red blood cell counts was noted. The degradation of

aging red blood cells is influenced by mechanical forces from foot strikes, muscle contractions, collisions with vessel walls, and gastrointestinal bleeding, all of which contribute to the decline in red blood cell numbers. Additionally, an increase in plasma volume can lead to decreased hematocrit levels; however, this condition reflects a reduction in blood concentration rather than a decrease in red blood cell count [66, 67].
Fasting and hunger can significantly affect hematological changes in the body, particularly in hemoglobin levels, hematocrit, and blood cell counts. Changes in nutrient intake and various physiological activities drive these effects. Specifically, levels of red blood cells and hemoglobin may be altered during fasting. Reduced food consumption can lead to changes in both hemoglobin and hematocrit levels. These changes vary among individuals, with some experiencing an increase and others a decrease in these markers [68]. The observed decrease in circulating hemoglobin concentration suggests that some athletes may have experienced over-hydration. This could be attributed to recommendations for increased water intake during the night or possibly to an expansion of the vascular space as a physiological adaptation to ongoing training [69, 70]. The alterations in hematological parameters were relatively minor, with all values remaining within the normal laboratory reference range, suggesting that Ramadan fasting did not adversely affect the hydration or iron levels of the athletes. The available data limit conclusions regarding immunological status. White blood cell (WBC) counts remained stable throughout Ramadan fasting. Further investigation into natural killer cell activity and immunoglobulin levels is warranted, as athletes are particularly susceptible to upper respiratory infections [71]. However, there is a lack of changes in WBC subsets, as noted by Chaouachi et al. [72], suggests that there is no evidence of viral or bacterial infections. Maughan et al. [40] Even reported a reduction in WBC counts among soccer players tested in the afternoon, which may indicate either hyperhydration or a diminished release of leukocytes from the bone marrow and other storage sites [73]. Importantly, all leukocyte parameters have remained within normal clinical ranges. Therefore, there is currently no evidence to suggest that maintaining training during Ramadan fasting compromises immune defenses.
Fasting combined with exercise training significantly decreased HOMA-IR (WMD: -1.65 [95% CI, -2.25 to -1.04]; p = 0.0001), but insulin levels and fasting blood glucose remained unchanged (WMD: 0.41 mg/dL [95% CI, -0.34 to 1.16], p = 0.28) following fasting and exercise training.
The results obtained from the present meta-analysis are consistent with the findings of Salse-Batán et al. [74], who investigated the effects of exercise and intermittent fasting on health in a systematic review. This study identified 4 RCTs with a total of 323 subjects. The results indicated that combining fasting with exercise improves body composition (e.g., weight, BMI, fat mass) and metabolic health markers such as glucose levels, insulin resistance, cholesterol, blood pressure, triglycerides, and oxygen uptake. Similarly, Yuan et al. [75] conducted a systematic review and meta-analysis to investigate the effects of exercise and intermittent fasting on health, identifying 10 RCTs with 359 subjects. The analysis revealed significant improvements in metabolic indicators: fasting blood glucose decreased by 0.15 mmol/L, glycosylated hemoglobin decreased by 0.08%, insulin levels decreased by 13.25 uUI, and insulin resistance, measured by HOMA-IR, decreased by 0.31. However, the present study's findings are inconsistent with those of Faris et al. [76], who conducted a meta-analysis evaluating the impact of Ramadan diurnal intermittent fasting (RDIF) on glucometabolic markers in healthy, non-athletic Muslims. Data from 72 studies across 22 countries (1982–2020) involving 3,134 participants were analyzed. The results showed minimal to no significant changes in fasting glucose, insulin, insulin resistance (HOMA-IR), leptin, and adiponectin, with effect sizes for fasting glucose (Hedges' g = -0.102), insulin (Hedges' g = 0.030), HOMA-IR (Hedges' g = -0.012), leptin (Hedges' g = -0.010), and adiponectin (Hedges' g = 0.034). The reduction in insulin levels suggests an improvement in insulin sensitivity. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) serves as a key index for insulin resistance and is widely regarded as the benchmark for assessing insulin sensitivity. An evaluation of insulin sensitivity following an intermittent fasting (IF) dietary intervention revealed an average decrease in

insulin levels (WMD: -1.65 [95% CI, -2.25 to -1.04]; p = 0.0001). This finding is comparable to clinical studies involving the oral insulin sensitizer pioglitazone [77], which reported an average reduction of 7.9 mU/L in fasting insulin levels and a decrease of 11.2 mU/L in 2-hour postprandial glucose after 16 weeks of pioglitazone administration. The extent of insulin reduction observed with the IF intervention parallels that achieved through oral insulin sensitization. While insulin sensitizers and dietary interventions lead to decreased insulin levels and improved insulin sensitivity, the pharmacological approach is often accompanied by adverse effects, such as weight gain, which can compromise long-term outcomes for patients with disrupted glucose and lipid metabolism. In contrast, dietary intervention alone has demonstrated the capacity to effectively enhance insulin sensitivity [78].

This study has several limitations that should be considered when evaluating the findings. First, the research exclusively included studies published in English despite employing an extensive search strategy. As a result, relevant studies published in other languages may have been overlooked. Another limitation is the variability in the timing and conditions under which blood hematological factors and insulin resistance markers were assessed across the included studies. This variability includes differences in the time of day for measurements and whether they were conducted in patients' homes or outpatient settings. Additionally, difficulties were encountered in obtaining certain studies for thorough analysis, despite efforts to contact the authors. The types of intermittent fasting examined in the trials also varied, as did the ethnic backgrounds of the participants, which hindered our ability to categorize studies by ethnicity or fasting type. Furthermore, among the studies analyzed, only five assessed insulin levels in participants, four evaluated HOMA-IR, and three measured white and red blood cell counts. This limitation prevented the possibility of grouping studies based on biomarker types. Future research is needed to enable more nuanced comparisons based on disease, ethnicity, intervention type, and duration. Focusing on more detailed aspects of the proposed protocols, study design, and precise scheduling can improve the clarity of future objectives. Given the ethnic and racial diversity within Muslim communities, emphasizing this diversity and conducting further research could lead to improved outcomes.

The strength of this study lies in its comprehensive analysis of the included research, which spans a diverse range of countries, enhancing the generalizability of the findings. This study is notable for its innovative approach, as it examines explicitly blood hematological factors and insulin resistance markers in adult Muslims.

## Conclusion

This meta-analysis confirms that various fasting modalities combined with exercise can significantly improve specific hematological parameters and markers of insulin resistance in adult Muslims. Intermittent fasting has gained popularity as a dietary approach to enhance body composition and metabolic health. This trend may be attributed to its effectiveness in promoting weight loss, reducing insulin resistance, and positively influencing blood hematological factors. However, further investigation is needed to thoroughly examine these factors and determine the most effective fasting and exercise protocols for maximizing health benefits in adult Muslims.

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