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Review

Foot-strike Hemolysis: A Scoping Review of Long-Distance Runners

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ABSTRACT

Objective. To investigate the role that foot-strike hemolysis plays in sports-related anemia in marathon and ultramarathon runners.

Data Sources. PubMed, Embase, Cochrane, Grey literature.

Study Selection. Inclusion criteria consisted of human studies with runners completing a sanctioned race of marathon distance or greater, with outcomes measured by pre- and post-race hematological assessments.

Data Extraction. Three independent reviewers systematically extracted data from selected studies. Data included age, sex, height, weight, best marathon time, and pre- and post-race outcomes for complete blood count, reticulocyte count, and iron studies. The evaluation of potential bias was conducted using the Methodological Index for Nonrandomized Studies (MINORS) criteria.

Data Synthesis. The literature search yielded 334 studies, of which nine met the inclusion criteria, encompassing data from 267 runners. The majority (88%, 236 out of 267) were male, with a weighted mean age of 37 years (SD 8.2). The reticulocyte count demonstrated a 16% increase between pre- and post-race measurements, although still within normal limits, while haptoglobin levels were reduced by 21%. Hemoglobin, hematocrit, and RBC count values remained within accepted normal limits.

Conclusions. Changes in reticulocyte count and haptoglobin levels suggest transient foot-strike hemolysis; however, hemoglobin and hematocrit levels did not change notably. It is unclear whether these associations are influenced by differences in runner demographics, running experience, or race characteristics. Further studies should evaluate hemolytic changes while matching participants by demographic characteristics, level of running experience, and specific marathon course characteristics. Additionally, research should analyze whether intravascular hemolysis occurs at race distances shorter than 42.2 km. ***Kans J Med 2024;17:119-125***

INTRODUCTION

In endurance runners, sports-related anemia has been described as commonplace. Various mechanisms are known to contribute to sports-related anemia, the most common of which is due to hemodilution secondary to a training-dependent increase in plasma volume.[1] Additional explanations for sports anemia include metabolic injury, exercise-induced oxidative stress, iron deficiency, gastrointestinal bleeding, hematuria, and direct mechanical injury to red blood cells (RBCs) due to repetitive and forceful impacts of the feet with the ground, known as foot-strike hemolysis.[1]

Foot-strike hemolysis, also known as march hemoglobinuria, was first described by Kast in 1884, detailing a 19-year-old man who developed gross hemoglobinuria after a prolonged period of marching.[2] Further studies have demonstrated exercise-induced intravascular hemolysis, conventionally diagnosed by an increased concentration of free hemoglobin in serum, decreased haptoglobin level, and reticulocytosis, as well as markers of cytolysis such as elevated levels of lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and unconjugated bilirubin.[3]

Sports anemia is generally transient and typically resolves within one to three months after discontinuing intensive exercise.[4] However, about 8% of elite athletes will develop frank anemia, defined as a hemoglobin concentration below 14.0 g/dL in males and 12.0 g/dL in females.[5] The precise contribution of foot-strike hemolysis to the development of sports anemia in long-distance runners has yet to be concretely defined. No systematic or scoping reviews have been published examining the current body of literature concerning this phenomenon to better determine the role, if any, that foot-strike hemolysis plays in sports-related anemia.

The goal of this scoping review was to quantitatively analyze the current available literature to summarize the existing body of literature surrounding foot-strike hemolysis and evaluate the hematologic effects following long distance runs of 42.2km (26.2 miles, the marathon distance) and greater.

METHODS

Search Strategy and Study Selection. Three independent authors (A.G., N.L., and N.D.) performed a scoping review of the literature following the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) guidelines (Figure 1).[6] The review was registered with the Prospective Register of Systematic Reviews (PROSPERO; [CRD42023454879]), and no similar meta-analyses or systematic reviews were identified. Databases utilized included PubMed, Embase, Cochrane, and a review of the grey literature. The electronic database search was performed through December 2023. The keywords used in the search, combined with the following Boolean operators included: "Foot strike hemolysis" OR "March hemoglobinuria" OR "Sports anemia" OR "Exercise-induced hemolysis" OR "Foot strike anemia". No filter was used during the database searches. All studies included were published, peer-reviewed articles. There were no specific timeline constraints regarding these publications. Appendix 1 provides further specific details regarding the location of PRISMA-ScR checklist items in the manuscript (appendix is only available online at journals.ku.edu/kjm).

Eligibility Criteria. All searches were extracted, and duplicate search results were discarded. Abstracts of each of the search results were screened to determine relevance. Articles were further excluded based on the following criteria: (1) non-English text, (2) full-length text

not available, (3) non-human study, (4) athletes did not run marathon length race (42.2 km) or longer, and (5) no pre-run and post-run hematological measurements. Studies that did not meet any of the exclusion criteria were included in the scoping review.

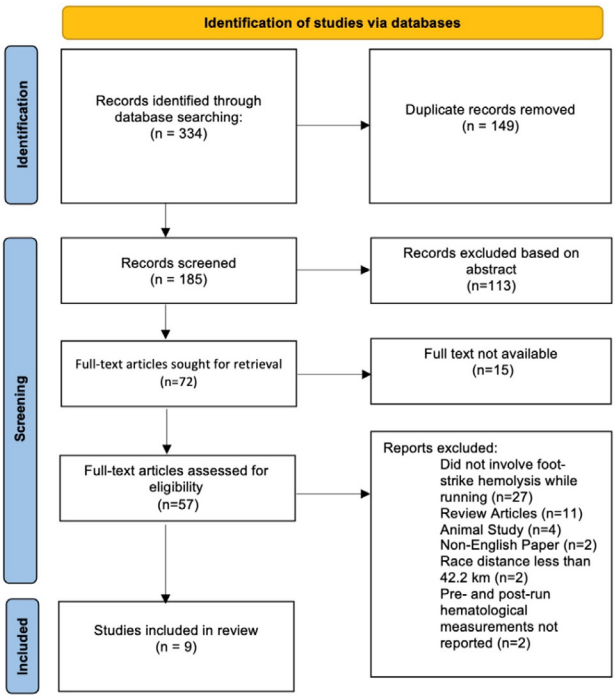

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart for studies included in scoping review.

Data Extraction. Data were extracted systematically from each selected study by a team of three independent reviewers (A.G., N.D., and N.L.). Data was cross-checked by each reviewer to limit bias and ensure accuracy. The outcomes sought during the data extraction phase consisted of a comprehensive set of data including demographic data, pre-race, and post-race outcomes. Demographic data included age, sex, height, weight, and best marathon time. Pre-race and post-race outcomes included a complete blood count, reticulocyte count, haptoglobin, and iron studies.

Risk of Bias Assessment. Potential bias was evaluated using the Methodological Index for Nonrandomized Studies (MINORS) criteria by two independent reviewers (A.G. and N.D). The MINORS is a validated instrument to assess the quality of non-randomized studies using a score between 0 and 16 (> 12 = high quality; 8 - 12 = intermediate quality; <8 = low quality) for noncomparative studies.[7] In the case of discrepancies in scoring, a third independent reviewer (N.L.) was utilized.

Statistical Analysis. Aggregate data from each study were summarized using weighted means and standard deviations for pre- and post-race follow-up measures. Weighting was based on sample size per study. Data also were summarized by race distance. Primary outcomes included hemoglobin, haptoglobin, and reticulocyte count.

RESULTS

The results of the comprehensive literature are displayed in Figure 1. A total of 334 studies were initially identified. After removing duplicate records, 185 remained. Another 15 were excluded due to unavailability of full-text articles. This process left 57 full-text articles to be assessed. Of these, 48 were excluded, resulting in nine studies being included in the review. The nine included studies consisted of a total of 267 runners. A summary of the characteristics of the studies included is presented in Table 1.

Most runners included in the study were male (n = 236), with a mean age of 38 years. The runners' mean best marathon time was 220 minutes. Race distance varied from study to study. Three studies examined races of marathon distance (42.2 km), three examined races between 42.2 km – 160 km, and two studies examined a one day and six-day ultra-marathon race, respectively. The overall average race distance was 54.4 km.

Baseline, follow-up and change in lab values were summarized as weighted means and are shown in Table 2. Change in lab values revealed three large increases: 45% increase in the ferritin level (ng/mL), from 93 at baseline to 135 at follow-up; 38% increase in platelet count (n*10^9/L), from 241 to 332; and a 16% increase in reticulocyte count (n*10^9/L), from 1.33 to 1.54. Two large decreases in lab values were observed: 28% decrease in the serum iron level (ug/d), from 103 at baseline to 74 at follow-up; and a 21% decrease in the haptoglobin level (g/L) 1.18 to 0.93. Despite changes in both reticulocyte count and haptoglobin level, hemoglobin levels, hematocrit, and RBC counts remained within accepted normal limits. The hemoglobin level increased by 1.1%; hematocrit by 0.2%; and RBC count by 1.7%, from 4.82 10^6/uL to 4.90 10^6/uL.

Table 3 summarizes the weighted mean change by race length. Race length varied by study, with the largest sample from 42.2 km race with 190 runners; only one runner was represented in the 160 km race. Weighted mean change also varied considerably; however, a few possible linear trends were observed: lab values for hemoglobin (g/dL) appeared to decline as length of race increased: from .30 increase at 42.2 km to a 1.50 decrease for the six-day race. Similarly, hematocrit (%) declined from a 1.43 increase down to 5.0 decrease. Conversely, ferritin (ng/mL) appeared to increase as race length increased: from 16 at 42.2 km to 129 for the six-day race. Lab values for both reticulocyte count (10^9/L) and haptoglobin (g/L) remained steady, regardless of race length.

Results of the bias assessment from MINORS are shown in Table 4. Reviewers found that all nine studies included in the analysis were of intermediate quality, with Score (Quality) ranging from 9 to 12. Studies lacked blind evaluation of the study endpoints (Q5) and power analyses to determine study size (Q8).

Table 1. Study characteristics.

Author	Year	Type of Study	Race Setting	Mean C°	Race Distance (km)	Total Runners	Mean Age	Sex (Male, Female)	Outcome Measures	Main findings
Chiu[1]	2015	Case Series	Taipei, Taiwan	26.8	100	25	47	(25,0)	Blood counts, free plasma hemoglobin, IL-6, TNF-alpha, Hs-CRP, EPO, and iron panel, 1 week before, immediately after, and 24 hours post-race	Hemoglobin rise immediately post-race, no changes in RDW, haptoglobin decrease immediately post-race with return to baseline at 24 hours, ferritin increase immediately post-race and 24 hours post-race
Davidson[12]	1987	Before-after	UK	11	42.2	135	32.7	(110,25)	Red cell, leukocyte, and platelet parameters, and haptoglobin 30 min pre-race and within 5-min post-race	Significant decrease in haptoglobin, RBC, Hgb, and an increase in ferritin and WBC count.
Fallon[8]	2002	Case Series	Colac, Australia	16	6 days	8	47	(7,1)	Red cell and reticulocyte parameters 30 minutes prior to race, each day of the 6-day race, and immediately post-race.	Haptoglobin decreased on day 1, elevated on day 3-6. Hemoglobin decrease day 2-6, Increase in percentage of reticulocytes with high RNA content
Kratz[9]	2006	Case Series	Boston, MA	21.1	42.2	32	49	(27,5)	Blood counts, reticulocyte counts, WBC differentials, platelet parameters, 36 hours before and immediately after race	Increase in WBC, hematocrit, and RBC count post-race. Increased hemoglobin and reticulocyte count. Elevated RBC fragments.
Lijnen[13]	1988	Case Series	Belgium	9.2	42.2	23	24.6	(23,0)	Blood counts, lactate, urine tests 8h, 2 h, and 5 minutes pre-race, and 12 h, 36 h, and 7 days post-race	LDH and myoglobin concentration increased, Haptoglobin decreased immediately and 12 hours post-race
Lippi[5]	2012	Case Series	n/a	7	60	18	42	(18,0)	Pre- and post-race hematological testing, creatine kinase (CK), albumin, AST, LDH	No statistically significant variations in hemoglobin, RBC count, and hematocrit. Haptoglobin and MCV significantly decreased, RDW increased.
Liu[11]	2018	Case Series	Taipei, Taiwan	20	24 hours	19	45	(19,0)	Blood counts, hemolysis markers, iron panel, and viscoelastic properties 1 week pre-race and immediately post-race	Haptoglobin, RBC count, plasma free hemoglobin decreased significantly. Reticulocyte and ferritin increased post-race.
Sanchis-Gomar[7]	2016	Case Report	Indoors	n/a	160	1	37	(1,0)	Blood counts, muscle and liver markers, iron metabolism, electrolytes, and metabolic markers 3 days before and 0, 24 and 48 hours postexercise	Increased post-exercise serum CK, AST/ALT, Bilirubin, Hemoglobin. RBC decline at 48 hours, increased ferritin at 24 and 48 hours.
Yusof[10]	1985	Case Series	Badwater Basin, CA	55	216	6	53.8	(6,0)	Hematocrit, hemoglobin, leukocyte count, EPO, protein, urinalysis, 1-hour pre-race, at 21, 42, 84, 126 km, and immediately after the race	Hemoglobin increased after 42 km compared with 216-km level. Haptoglobin decreased during the initial 84 km. Spectrins reduced throughout the race.

Table 2. Baseline and follow-up weighted means including laboratory values.

Variable	n	Baseline	Follow-up	Change	%
		$Mean_{wgt}$ (SD)	$Mean_{wgt}$ (SD)	$Mean_{wgt}$	Change
Height (m)	185	1.73 (0.06)	--	--	
Weight (kg)	216	68.14 (7.51)	--	--	
Best marathon time (min)	210	219.41 (34.24)	--	--	
Hemoglobin (g/dL)	267	14.17 (1.06)	14.33 (0.97)	0.16	+1.13
Hematocrit (%)	132	44.01 (2.43	44.09 (2.88)	0.07	+0.18
RBC (10^6/uL)	267	4.82 (0.34)	4.9 (0.35)	0.07	+1.66
MCV (fl)	244	90.3 (4.05)	90.49 (4.10)	0.20	+0.21
MCH (pg)	244	30.41 (1.52)	30.32 (1.58)	-0.09	-0.30
MCHC (g/dL)	244	33.77 (0.77)	33.47 (0.89)	-0.33	-0.89
RDW (%)	238	11.76 (0.82)	12.16 (1.97)	0.46	+3.40
Reticulocyte count (n*10^9/L)	59	1.33 (0.42)	1.54 (0.47)	0.21	+15.79
Platelet count (n*10^9/L)	193	240.98 (52.99)	331.83 (63.72)	90.84	+37.70
Haptoglobin (g/L)	214	1.18 (0.49)	0.93 (0.50)	-0.26	-21.19
Iron (µg/d)	53	103.23 (36.93)	73.92 (34.04)	-29.31	-28.39
Ferritin (ng/mL)	78	93.43 (69.82)	135.04 (104.62)	41.60	+44.54

% Change = [(Follow-up – Baseline)/Baseline] * 100
Normal lab values by sex:
- Hemoglobin: 13.6 - 16.9 g/dL for males; 11.9 - 14.8 g/dL for females.
- Hematocrit: 40 - 50% for males; 35 - 43% for females
- Red blood cell count (RBC): 4.2 - 5.7 * 10^6/microL for males; 3.8 - 5.0 * 10^6/microL for females
- Mean corpuscular volume (MCV): males and females, 82.5 - 98 fL
- Mean corpuscular hemoglobin (MCH): males and females, 27.6 - 33.3pg.
- Mean corpuscular hemoglobin concentration (MCHC): males and females, 32.5 - 35.2 g/dL
- Red blood cell distribution width (RDW): males and females, 11.4 - 13.5%.
- Reticulocyte count: 16 - 130 * 10^9/L for males; 16- 98 * 10^9/L for females.
- Platelet count: 152- 324 *10^3/microL for males; 153- 361 *10^3/microL for females
- Haptoglobin: males and females, 50-220 mg/dL or 0.5-2.2 g/L
- Iron: 65 to 176 µg/dL for males; 50 to 170 µg/dL for females
- Ferritin: 12–300 nanograms per milliliter (ng/mL) for males; 12–150 ng/mL for females

Table 3. Weighted mean change by race length.*

Variable	Race Length						
	42.2 km	60 km	100 km	160 km	216 km	24-hour race†	6-day race†
Population (n)	190	18	25	1	6	19	8
Weighted mean change							
Hemoglobin (g/dL)	0.30	0.10	0.40	-0.60	-0.48	-0.50	-1.50
Hematocrit (%)	1.43	-0.57	0.90	-2.20	-2.00	-1.43	-5.00
RBC (10^6/uL)	0.14	-0.07	0.10	-0.23	-0.18	-0.17	-0.53
MCV (fl)	0.49	-1.43	0.40	0.00	-0.58	-0.50	-0.50
MCH (pg)	-0.17	0.00	0.30	0.10	0.26	-0.30	0.40
MCHC (g/dL)	-0.55	0.50	0.20	0.20	0.58	-0.17	0.60
RDW (%)	0.59	0.07	0.00	-0.30	0.00	0.07	-0.50
Reticulocyte count (10^9/L)	0.20	0.00	0.00	0.00	0.00	0.20	0.30
Reticulocyte count (10^9/L)	99.54	0.00	38.30	-48.00	0.00	0.00	0.00
Haptoglobin (g/L)	-0.41	-0.30	0.38	0.00	-0.23	-0.50	1.00
Iron (ug/dL)	0.00	0.00	-54.10	6.00	0.00	15.67	-63.10
Ferritin (ng/mL)	16.00	0.00	42.80	52.70	0.00	36.33	129.00

Note: RBC, Red blood cell count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red blood cell distribution width.
*Values represent differences calculated between baseline and follow-up weighted means
† 24-hour and 6-day races were time-based rather than distance-based races.

Table 4. MINORS criteria assessment of bias.

Author (Year)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Score (Quality)
Chiu (2015)[1]	2	2	2	1	0	2	1	0	10 (Intermediate)
Davidson (1987)[8]	2	0	2	1	0	2	2	0	9 (Intermediate)
Fallon (2022)[9]	2	1	2	2	0	2	1	0	10 (Intermediate)
Kratz (2006)[10]	2	2	2	2	0	2	2	0	12 (Intermediate)
Lijnen (1988)[11]	2	2	2	2	0	2	2	0	12 (Intermediate)
Lippi (2012)[5]	2	1	2	2	0	2	2	0	11 (Intermediate)
Liu (2018)[12]	2	1	2	1	0	2	1	0	9 (Intermediate)
Sanchis-Gomar (2016)[13]	2	0	2	1	0	2	2	0	9 (Intermediate)
Yusof (1985)[14]	2	1	2	2	0	2	2	0	11 (Intermediate)

Rating per question: 0 = not reported, 1= reported but inadequate, 2= reported and adequate
Score (Quality): >12 = high, 8-12 = intermediate, < 8 = low
Q1: Clearly state aim
Q2: Inclusion of consecutive patients
Q3: Prospective collection of data
Q4: Appropriate endpoints
Q5: Unbiased assessment of endpoints
Q6: Appropriate follow-up period
Q7: Loss to follow-up less than 5%
Q8: Prospective calculation of study size

DISCUSSION

The sport of running has surged in popularity over the past decade, with races attracting 108 million participants across 70,000 events in 2019.[17] The COVID-19 pandemic has further amplified the sport of running, with runners increasing their mileage and number of runs per week significantly.[18] Given this rise in popularity, understanding the mechanisms by which sports anemia occur is integral for effective treatment and prevention, helping to avoid injury and improve running performance.

Our study findings provide valuable insights into the potential effects of foot-strike hemolysis on marathon runners. Hemolysis is primarily indicated by a decreased haptoglobin level, which was evident in this study. Haptoglobin is a molecule whose function is to complex with free hemoglobin when intravascular destruction of erythrocytes occurs, allowing for the recycling of both the hemoglobin and iron intrahepatically.[19] In the present study, haptoglobin levels were reduced by 21% between pre- and post-race weighted means. In most cases, despite a reduction in the haptoglobin level suggestive of intravascular hemolysis, clinically apparent hemoglobinuria did not occur.

Evaluation of RBC Parameters. An increase in the mean reticulocyte count was found, consistent with the human body's physiologic response to RBC breakdown, although mean values were still within normal levels. Variability in the reticulocyte count has been noted as commonplace. Increased red blood cell turnover has been described following various race distances, including short training runs, marathons, ultramarathons, and triathlons.[9] One theory for reticulocyte response variability is that present-day shoe materials have attenuated the severity of foot-strike hemolysis, thus leading to a diminished reticulocyte response.[3] Telford et al.[20] described reticulocyte levels that were 29% higher in runners training with hard-soled shoes running 429 km in 18 days, compared with a matched control group of soft-soled shoes. The lack of significant clinical effects or critical changes to the haptoglobin level and reticulocyte count may be attributable to pre-race physiologic adaptations. The average runner in the systematic review had a best marathon time of 220 minutes and was running an average of 54.4 km per week prior to the study. This appreciable training stimulus likely allows for the attenuation of substantial effects to the body, as these well-trained athletes had already reached a stable erythropoietic response.[5]

The study participants' mean hemoglobin level increased slightly from 14.17 to 14.33 g/dL, a 1.1% increase, with hematocrit also increasing slightly but remaining within normal limits. The pre-race hemoglobin of ~14 g/dL is evidence that the average runner in the study did not begin their respective race with traditionally defined anemia. The lack of significant change after undergoing an endurance race may be attributable to physiologic adaptations. However, it is plausible that hemoconcentration contributed to the increase of these values, as dehydration is commonplace in endurance running races.[21] In general, exhaustive endurance exercise initially causes volume contraction due body fluid loss, with subsequent volume expansion between 6 - 25%. The mechanism of this volume expansion is not entirely known but is likely due to activation of the renin-angiotensin-aldosterone (RAAS) system along with the osmotic regulation of vasopressin. In most cases, labs were taken immediately after the race, likely prior to the body's ability to recover from dehydrative effects.[19] Chiu et al.[1] looked at anemia in male 100 km ultramarathon runners. An analysis of hematological parameters immediately post-race as well as 24 hours post-race found mean hemoglobin levels of 14.7 ± 0.8 and 13.6 ± 0.8, respectively.

The foot-strike hemolysis phenomenon can be additionally supported by the increased red blood cell distribution width (RDW). RDW is a routine measure of variability in the size of circulating erythrocytes. RDW commonly is increased in nutritional deficiencies, such as iron, B12, and folate deficiency. Hemolysis results in reticulocytosis due to the body's attempt to compensate for erythrocyte losses. Due to the size disparity between reticulocytes and mature erythrocytes, RDW typically is elevated in cases of reticulocytosis.[22]

Evaluation of Iron Stores. The evaluation of iron and ferritin level changes is complex due to various factors influencing these parameters. It is well known that long-distance running can lead to depletion of iron stores. Some reasons for this include hemolysis, hematuria, sweating, and inflammation stimulating hepcidin production.[23] Because the intestinal absorption of iron is low (heme iron showing 15 - 25% absorption, with nonheme iron showing only 2 - 5% absorption), iron deficiency is common.[24] In the present study, iron levels were substantially reduced by 28%, from 103.23 ug/dL to 73.92 ug/dL. Ferritin levels, on the other hand, increased by 44.5% from 93.43 ng/mL to 135.04 ng/mL. In many cases, ferritin levels are decreased in trained individuals due to increased iron turnover and cell destruction from running. However, as stated previously, the effects of hemoconcentration likely play a role in the increased levels seen.[25] In addition, runners who already were taking iron supplementation prior to the study may have artificially elevated levels of ferritin. Despite substantial changes in iron levels, clinical manifestations associated with these changes were not present.

Oxidative Stress. Several confounding factors exist that may play a role in erythrocyte injury as it relates to physical exercise. Exercise-induced oxidative stress has been noted to occur in several athletic non-traumatic endeavors such as swimming, cycling, and rowing.[5] One of the primary mechanisms of this process relates to increased oxygen uptake into skeletal muscle which facilitates the generation of reactive oxygen species (ROS) and free radicals. Factors contributing to this increased ROS production include cellular pH changes, body temperature alterations, and catecholamine production.[26]

Limitations. The study has several limitations. First, the lack of quantitative research on foot-strike hemolysis limits the ability to make generalizable conclusions and impacted heterogeneity. Much of this variability can be attributable to intrinsic race characteristics, including race surface and conditions, which may significantly affect the amount of hemolysis.

Another limitation is the variability in runner demographics. Many runner characteristics have not been described in previous studies, including experience, hydration status, and nutrition. Additionally, some argue that new shoe technology has significantly reduced the

hemolytic effects of repeated foot striking.[5]

Another limitation is the lack of statistical evaluation for pre-post differences. We chose not to conduct such tests, as there is a potential bias in utilizing pre-post mean differences. This bias may stem from lack of control group, along with differences in measurement, and study design. While a standardized mean score might account for differences in measurement, there is no control group for comparing these calculations. Therefore, an inherent correlation between the pre- and post-test data exists, which may result in biased outcomes.[27] Future studies may want to consider utilizing MA-CONT, a more robust way to analyze continuous outcomes.[28]

Lastly, studies like Yusof et al.[14] discuss that exercise-induced hemolysis is more prominent in the early stages of an endurance race, likely secondary to preferential removal of older red blood cells via splenic filtration rather than intravascular hemolysis. Unfortunately, few studies have examined early race RBC damages due to the logistical challenges of conducting such research.

CONCLUSIONS

Changes in reticulocyte count and haptoglobin suggest a transient foot-strike hemolysis, though hemoglobin and hematocrit did not change notably. These findings may be attributable to dehydration, advances in shoe technology, or physiological adaptations in endurance athletes. Future studies should evaluate hemolytic changes while matching participants by demographic characteristics, level of running experience, and specific marathon course characteristics as well as investigating intravascular hemolysis distances shorter than 42.2 km.

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