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Original Research

Depression in Collegiate Runners and Soccer Players: Relationships with Serum 25-Hydroxyvitamin D, Ferritin, and Fractures

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ABSTRACT

International Journal of Exercise Science 14(5): 1099-1111, 2021. The main purpose of this study was to evaluate relationships between depression versus serum 25-hydroxyvitamin D (vitamin D), serum ferritin (ferritin), and fractures across a competitive season. The authors conducted a prospective observational study (both pre- and post-season testing) on 51 collegiate soccer and cross-country athletes from a Midwest University. Our main outcome measure was depression, measured using the Center for Epidemiological Studies Depression Scale (CES-D). A CES-D score ≥ 16 represented the threshold value for clinical depression. Secondary outcome variables included vitamin D, ferritin, and fractures. Two athletes (3.9%; one female) pre-season while seven athletes (13.7%; five females) post-season demonstrated clinically relevant depression (CES-D score ≥ 16). Depression scores increased from pre- to post-season (6.0 to 8.9; $p = 0.009$; effect size = 0.53; $n = 51$). A medium effect noted for depressed athletes vs. non-depressed athletes ($n = 7$; post-season) to have lower pre-season serum vitamin D (38.4 vs. 50.2 ng/ml; $p = 0.15$; effect size = 0.68) with a small overall correlation effect ($r = -0.08$; $p = 0.58$). A medium correlation effect was noted between post-season ferritin vs. depression scores ($r = -0.45$; $p = 0.01$) in the female cohort only. Six athletes (11.8%) sustained fractures and had lower depression scores vs. non-injured athletes (4 vs. 10; $p = 0.04$; effect size = 1.08) post-season. Depression scores increased over a competitive season, especially in females. Small correlation effects were observed between depression and vitamin D. A medium correlation effect was noted between depression and low ferritin levels, in female athletes only. A large effect was noted between athletes sustaining fractures during the season and depression, post-season, with injured athletes being less depressed than non-injured athletes.

KEY WORDS: Vitamin D, athletes, mental health, CES-D

INTRODUCTION

Depression or major depressive disorder is a mood disorder that negatively affects how an individual feels, thinks and acts (2). This multifaceted disorder is characterized by persistent (≥

two weeks) sadness, fatigue, loss of interest in usually enjoyable activities (anhedonia), feelings of worthlessness, difficulty thinking or concentrating, changes in appetite or sleep patterns, indecisiveness, and/or thoughts of death (1, 2). Currently, depression affects nearly 4.7% adults in the United States (7). The incidence of depression appears much higher among University students, however, ranging between 10% and 85% (13).

Participation in sports is thought to reduce depression, through complex biological and psychosocial mechanisms associated with regular physical activity (15, 25). The anti-depressive effects of collegiate sports, however, appears more complex (34). Large cross-sectional studies investigating the prevalence of depression, using the Center for Epidemiological Studies Depression Scale (CES-D), identified clinically relevant depression in 21-23.7% of National Collegiate Athletic Association Division 1 (NCAA D1) student-athletes surveyed (34, 35). The prevalence of depression appears highest in male and female track and field athletes (35.4%) and female soccer players (31%) (34). Females are consistently more likely to report depressive symptoms (34, 35) while males are at greater risk of suicide (27).

Vitamin D (assessed in the blood as the inactive metabolite, serum 25-hydroxyvitamin D or "vitamin D" for short) is thought to attenuate depression by stimulating brain serotonin levels (30), reducing inflammation (11), and/or enhancing the biosynthesis of key neurotransmitters during brain development (3). Clinical investigations performed on non-athletes demonstrate an inverse relationship between depression scores and vitamin D (26). A cross-sectional sample of 615 healthy university students suggested those students with the lowest serum vitamin D (by quartile) reported a greater number of depressive symptoms (26). Furthermore, for every one standard deviation increase in serum vitamin D (27 nmol/L), there was a 4.5 point increase in CES-D score (26). In another study, conducted on 40 adolescent females, vitamin D_3 supplementation reduced depression scores after a nine-week intervention (3). Collectively, these studies support a possible relationship between depression and vitamin D levels in healthy young individuals.

Ferritin (assessed in the blood as the inactive iron-carrier protein, serum ferritin or "ferritin" for short) is thought to reflect tissue iron stores (16). Ferritin levels are commonly used as an early indicator of iron deficiency or anemia with signs and symptoms which may overlap with those of depression (i.e. fatigue and poor performance) (5, 8, 23, 28). As such, depression has also been associated with low ferritin levels, particularly in young females (33). In a case-controlled study performed on 192 female medical students, logistic regression analyses estimated that the odds of depression increased by 1.92 when females with normal ferritin levels experienced a decline in ferritin levels below the low ferritin threshold (≤ 15 ng/L) (33). With the prevalence of iron depletion in female athletes between 16% and 57%, decreases in serum ferritin may substantially increase depression rates in female student-athletes with unknown effects on male athletes (23).

Lastly, it is unclear whether or not depression can lead to injuries or result from injury (1, 31). Biochemically, low vitamin D levels have been implicated in bone disease (12), while ferritin has not. In active populations, a relationship between low vitamin D levels and fracture risk has been described in male military recruits (20). Similarly, stress fractures are higher in female recruits with iron deficiency (36). Thus, the influence of depression, vitamin D and/or ferritin on fracture risk in athletes remains underexplored.

The primary aim of this investigation was to assess changes in depression and potential associations between depression versus serum vitamin D and ferritin levels across a competitive season in NCAA D1 runners and soccer players. We hypothesized that student-athletes with lower serum vitamin D and/or lower serum ferritin levels would demonstrate higher depression scores. An exploratory aim was to compare depression scores, serum vitamin D and ferritin levels in athletes who sustained fractures versus athletes who did not sustain fractures across a single season. The clinical relevance of any significant association between depression with serum vitamin D and/or ferritin, may support future implementation of nutrient supplementation (vitamin D or iron supplements) aimed at attenuating depression and/or fracture risk in runners and soccer players across a competitive season.

METHODS

Participants

All male and female members from a Midwestern NCAA D1 (latitude 42° N) soccer and cross-country (XC running) team were recruited to participate in this prospective, observational, study. Inclusion criteria included any student-athlete eligible to compete on the University's soccer or XC running team that season, without a history of fainting during blood draws. All eligible participants were recruited (and tested) during the first week of pre-season practice (August).

66 of 69 eligible athletes agreed to participate and signed written informed consent for this IRB-approved study. Pre-season testing was conducted during the first week of official practice (August), prior to the start of Fall semester classes and official competition. Post-season testing was conducted in December, 3 - 4 weeks following the completion of each team's respective season and one week prior to final exams. All researchers complied with the stated ethical statements and requirements set forth by the International Journal of Exercise Science's official Position Stand (22).

Protocol

For both pre-season and post-season testing, all participants presented to the research laboratory, prior to practice, in a non-fasted condition. All athletes completed the depression screening (pen and paper) and had their blood drawn (5 mL) via venipuncture, in a supine position, by a trained phlebotomist (EE) for measurement of vitamin D and ferritin levels. All fractures that were sustained during the competitive season were verified and recorded by the athletic trainer (JC).

Depression was assessed using a validated 20-question CES-D symptom scale. This scale was designed to assess depressed affect, positive affect, somatic vegetative signs, and interpersonal distress. The range of possible scores is 0 - 60, with higher scores reflecting greater depressive symptoms. Clinical depression was defined by a CES-D score of 16 or higher (26, 34, 35).

Venous blood samples were collected in serum separator tubes, allowed to clot for 20 minutes, and then centrifuged for 15 minutes. After centrifugation, serum was aliquoted into labelled Eppendorf tubes, refrigerated, and transported to the hospital laboratory (within 6 hours of collection) for analyses of serum 25-hydroxyvitamin D and serum ferritin levels (Cobas E Immunoassay, Ascension-Crittenton Hospital, Rochester, Michigan).

Statistical Analysis
Statistical analyses were performed using paired and unpaired t-tests. Simple regression analyses were used to assess relationships between depression with biomarkers (serum vitamin D and ferritin). Effect sizes, to determine magnitude of effects (14), were calculated using Cohen's *d* (32), with small (0.2), medium (0.5), and large (0.8) magnitude of effects (defined) for both t-tests and regression correlations (Pearson's r) (32). Post-hoc power calculations were also calculated for the primary variables of interest: depression (CES-D) = 99.3% power (mean population = 14, mean study group = 6, subjects study group = 51, $a = 0.05$) (26); serum vitamin D = 100% power (mean population = 64.1 ng/ml, mean study group = 48 ng/ml, subjects study group = 51, $a = 0.05$) (26); and serum ferritin for females = 93.6% power (mean population = 34.8 ng/ml, mean study group = 50.2 ng/ml, subjects study group = 29; $a = 0.05$) (19). All data reported as the mean ± SD.

RESULTS

Fifty-one of 66 (77%) consenting soccer and cross-country athletes completed both pre-season and post-season testing with a full dataset for analyses. For the combined cohort, a pre- to post-season increase in depression score was noted, of medium magnitude of effect (6.0 to 8.9; $p = 0.009$; effect size = 0.53). A pre- to post-season decreases in serum vitamin D was noted, of small magnitude of effect (48.6 ng/ml to 43.3ng/ml; $p = 0.16$; effect size = 0.28), Lastly, a decrease in serum ferritin was noted with no magnitude of effect (71.4 ng/ml to 70.0 ng/ml; $p = 0.89$; effect size = 0.03).

Table 1 summarizes demographic (age and body mass index/BMI) and main outcome variables in the combined cohort ($N = 51$), further subdivided by sex (29 females and 22 males). A large effect size (Cohen's $d > 0.8$) was noted between female versus male athletes for pre-season ferritin levels, with moderate effect sizes noted for post-season, %Δ in ferritin, and BMI between sexes.

Table 1: Combined data (*N* = 51) also divided by sex.

Variable	Combined (*N* = 51)	Females (*N* = 29)	Males (*N* = 22)	*p*-value	Cohen's *d*
Pre-CES-D	6.0 ± 4.1	6.1 ± 3.6	5.9 ± 4.6	0.86	0.05
Post-CES-D	8.9 ± 6.5	8.8 ± 6.7	9.0 ± 6.4	0.94	0.03
%Δ CES-D	222.9 ± 968.0	103.6 ± 201.4	380.1 ± 1460.0	0.32	0.27
Pre-Vitamin D (ng/mL)	48.6 ± 20.0	50.9 ± 22.0	45.5 ± 17.2	0.35	0.27
Post-Vitamin D (ng/mL)	43.3 ± 18.1	46.8 ± 20.2	38.7 ± 14.1	0.11	0.47
%Δ Vitamin D (ng/mL)	-8.5 ± 22.3	-5.5 ± 21.1	-12.4 ± 23.6	0.28	0.31
Pre-Ferritin (ng/mL)	71.4 ± 56.5	50.2 ± 37.8	99.2 ± 65.3	0.001	0.92
Post-Ferritin (ng/mL)	70.0 ± 45.7	60.2 ± 37.1	83.0 ± 53.1	0.07	0.50
%Δ Ferritin (ng/mL)	26.0 ± 85.3	46.8 ± 94.3	-1.4 ± 64.2	0.04	0.60
Age (years)	20.0 ± 1.4	19.8 ± 1.4	20.3 ± 1.5	0.21	0.34
BMI (kg/m^2)	22.6 ± 2.2	22.0 ± 2.2	23.3 ± 1.9	0.02	0.63

The magnitude of difference between female versus male athletes are demonstrated using both p-value's (from unpaired t-tests) and effect size (from Cohen's d). The %Δ value calculated as: (post-season minus pre-season)/pre-season x 100. CES-D =The Center for Epidemiologic Studies Depression scale score; Vitamin D = serum 25-OH vitamin D concentration. Ferritin = serum ferritin concentration; BMI = body mass index.

Table 2 summarizes the main outcome variables, separated by sport. Very large (Cohen's *d* > 0.8) were noted between XC runners and soccer players for pre-season vitamin D, %Δ in vitamin D, and BMI.

Table 2: Comparisons between sports (soccer versus cross country/XC Running).

Variable	XC Running (*N* = 20)	Soccer (*N* = 31)	*p*-value	Cohen's *d*
Pre-CES-D	4.9 ±2.9	6.7±4.6	0.11	0.47
Post-CES-D	7.8 ±6.2	9.6±6.7	0.33	0.28
%Δ CES-D	123.0 ±223.8	287.4±1232.6	0.56	0.19
Pre-Vitamin D (ng/mL)	61.6 ±18.8	40.2±16.1	<0.001	1.22
Post-Vitamin D (ng/mL)	45.8 ±15.7	41.7±19.6	0.44	0.23
%Δ Vitamin D (ng/mL)	-25.4 ±9.0	2.4±21.4	<0.001	1.69
Pre-Ferritin (ng/mL)	63.9 ±37.0	76.1±66.3	0.46	0.22
Post-Ferritin (ng/mL)	64.9 ±31.5	73.3±53.1	0.52	0.19
%Δ Ferritin (ng/mL)	26.5 ±74.0	25.7±93.1	0.97	0.01
Age (years)	20.0 ±1.8	20.0±1.1	0.90	0.00
BMI (kg/m^2)	21.0 ± 1.6	23.6±1.9	<0.001	1.48

The magnitude of difference between XC Runners versus Soccer players are demonstrated using both p-value's (from unpaired t-tests) and effect size (from Cohen's d). The %Δ value calculated as: (post-season minus pre-season)/pre-season x 100.

Two athletes (one male, one female; 3.9%) demonstrated clinically relevant (CES-D ≥16) depression pre-season (19.5 ± 4.9), which persisted into post-season (21.0 ± 7.1). These two participants had lower vitamin D levels pre-season (28.0 ± 0.2 vs. 49.4 ± 20.0 ng/mL; $p = 0.13$; effect size = 1.52) and post-season (27.7 ± 0.9 vs. 43.9 ± 18.2 ng/mL; $p = 0.21$; effect size = 1.27) (non-depressed vs. depressed athletes, respectively). Pre-season ferritin (81.8 ± 60.0 ng/mL) and post-season ferritin (75.2 ± 63.9 ng/mL) levels were within normal limits for these two athletes and neither participant sustained a fracture during the season.

Seven athletes (two males, five females; 13.7%) demonstrated depression post-season, with medium magnitudes of effect for both lower pre-season serum vitamin D and ferritin (Table 3).

Table 3: Comparison of student-athletes without clinical depression (CES-D <16) and those with clinical depression (CES-D ≥16) during post-season testing.

Variable	CES-D < 16 (*n* = 44; 24 females)	CES-D ≥ 16 (*n* = 7; 5 females)	*p*-value	Cohen's *d*
Pre-CES-D	5.5 ± 3.1	9.4±7.2	0.01	0.70
Post-CES-D	6.9 ± 4.1	21.3±4.4	<0.001	3.39
%Δ CES-D	224.3 ± 1042.4	214.0±145.3	0.98	0.01
Pre-Vitamin D (ng/mL)	50.2 ± 20.6	38.4±13.1	0.15	0.68
Post-Vitamin D (ng/mL)	44.3 ± 19.1	37.1±8.6	0.34	0.49
%Δ Vitamin D (ng/mL)	-10.0 ± 22.0	0.9±23.2	0.23	0.48
Pre-Ferritin (ng/mL)	74.8 ± 58.7	49.9±35.8	0.28	0.51
Post-Ferritin (ng/mL)	72.2 ± 47.1	56.5±35.2	0.40	0.37
%Δ Ferritin (ng/mL)	26.1 ± 89.3	25.7±59.3	0.99	0.01

The magnitude of difference is demonstrated using both p-value's (from unpaired t-tests) and effect size (from Cohen's d). The %Δ value calculated as: (post-season minus pre-season)/pre-season x 100.

There were inverse relationships between serum vitamin D vs. CES-D scores pre-season (Figure 1a) and post-season (Figure 1b), with small magnitudes of effect. An inverse relationship was found between post-season serum ferritin vs. post-season CES-D scores in the female cohort only (Figure 1c), with a medium magnitude of effect. There were no other meaningful relationships noted between depression scores, serum vitamin D, and/or serum ferritin levels pre- or post-season (in males, females, or combined cohorts).

Six athletes (one male; 11.8%) sustained season-ending fractures during the competitive season. The injured vs. non-injured athletes demonstrated *decreased* depression scores both pre-season (3.5 vs. 6.3; p = 0.10; effect size = 0.77) and post-season (3.8 vs. 9.5; p = 0.04; effect size = 1.08) with large magnitudes of effect. There was no magnitude of effects noted between athletes with fractures vs. athletes without fractures in serum vitamin D or serum ferritin levels pre-season, post-season, or Δ (post minus pre-season).

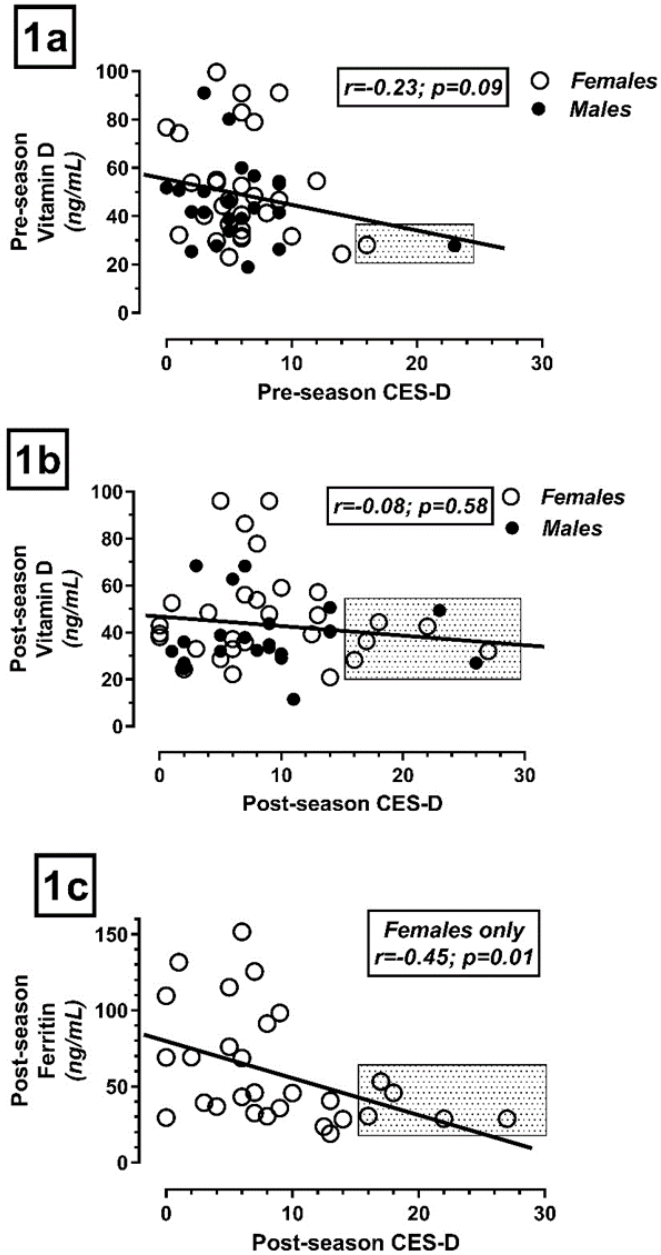

Figure 1. : Relationships between Vitamin D vs. CES-D pre-season (1a) and post-season (1b) and between ferritin vs. CES-D score post-season for female athletes only (1c). The athletes with depression are represented within the shaded boxes.

DISCUSSION

Our pre-season (3.9%) and post-season (13.7%) combined incidence of depression in soccer and cross-country athletes was lower than previously reported (21 - 23.7% overall incidence) in NCAA D1 athletes, using the same depression scale (34, 35). One possible reason for the difference was the timing of the screening, as one study conducted the CES-D screening in May (34), while the other conducted it "pre-season"(35). Our depression scores significantly increased across the season regardless of competitive outcome (i.e., the soccer teams had a losing season while the cross-country teams won the championship). Furthermore, pre-season testing was performed before classes started while post-testing was performed the week before final exams which may have triggered a stress-induced increase in depression symptoms at the end of the semester. Of note, the %Δ in CES-D between clinically depressed (CES-D ≥ 16) and non-depressed (CES-D < 16) participants were similar (i.e., an increase of ~200% across both groups) (Table 3). This suggests that clinical depression, when detected at baseline, is more likely persistent (major depressive disorder, rather than a transient mood shift) that is equally magnified by environmental stressors. However, the overall increase in depression amongst participants underscores the need for clinicians to identify depressed athletes early (i.e., perform baseline screenings), have mental health counseling freely available, and expect depression scores to increase across the competitive season when coupled with school stressors.

Unlike larger studies performed on 615 University students (26) and 178 prenatal African American women (6), no significant negative relationships were noted between serum vitamin D levels and depression scores either pre- or post-season in our small cohort of collegiate runners and soccer players. Our preliminary relationships demonstrated small magnitudes of effect perhaps because our sample size was too small (N = 51) for the hypothesized inverse association to have higher magnitudes of effect. Interestingly, our two athletes who met the CES-D criteria for depression pre-season tended to have lower serum vitamin D levels (28.0 ± 0.2 ng/mL) than their non-depressed teammates (49.4 ± 20.0 ng/mL); just below the threshold (< 30 ng/mL) for 25-hydroxyvitamin D insufficiency (12). As such, future investigations should consider examining the potential attenuating effects of high dose vitamin D supplementation on depression before and during the competitive season in student-athletes in future.

The present study did reveal a significant (moderate magnitude of effect) inverse relationship between serum ferritin vs. depression scores post-season in the female cohort only (Figure 1c). Low tissue ferritin stores are considered a precursor for iron deficiency anemia, which clearly affects endurance performance and performance perception in pre-menopausal female athletes (24, 28). This relationship was not seen in our male athletes, as males typically have higher ferritin levels (i.e., no menstrual blood losses) (5) and performance decrements are not seen in males until ferritin levels drop below 50 ng/mL (8). Of note, monthly menstrual blood losses are typically between 60 - 100 mL (10), with mathematical models confirming linear relationships between menstrual blood loss with decreases in ferritin and hemoglobin levels (29). Thus, menstrual blood losses place female athletes at greater risk for low iron stores and iron deficiency anemia.

The ferritin levels documented in our athletes post-season (Table 1) (Figure 1c) were largely not within the range of insufficiency, defined as serum ferritin levels below 30 ng/mL in the absence of systemic inflammation (5). Iron is thought to mediate depressed mood through its actions on dopamine synthesis and oxygenation of brain parenchyma (33), particularly during times of rapid growth where higher amounts of iron are required to accommodate increased metabolism (21). Although wide variability exists between depression scores and serum ferritin levels in our female cohort post-season, it is tempting to speculate on the (potential) positive value of iron supplementation on improving depression, mood and cognition in female athletes in future (4, 21, 33). However, we cannot rule out the potential influence of pre-menstrual syndrome (PMS) on depression scores, as previously documented in a cohort of female soccer players (9). The lack of a relationship between depression scores and ferritin levels pre-season highlights the underlying complexity between biochemistry, genetics, personality, and environmental factors which trigger depression (2).

Lastly, the six athletes who sustained season-ending fractures unexpectedly demonstrated lower depression scores both pre- and post-season. An association between anxiety, and not depression, was found in another study assessing injury rates in collegiate athletes (18). We anticipated that fractures would be associated with higher depression scores, as depression scores were significantly higher in injured athletes versus both non-injured athletes and healthy controls in prior studies (1, 17). We speculate that enough time had passed post-injury to normalize any transient increase in depression, in our injured athletes (back to baseline levels) (1). However, our sample size was too small and the injury timeline too varied to support further critical analyses to support this highly speculative assumption. There were no significant differences in either serum vitamin D or ferritin in athletes sustaining fractures (versus athletes without fractures) during the season. Thus, we believe the traumatic and/or biomechanical nature of these fractures superseded any mental or biochemical derangements in our (small) sample of athletes who sustained bone injuries during the competitive season.

There were several limitations to this observational study, in addition to limited sample size and modest dropout rate (23%; mostly male soccer players). First, the timing of the questionnaire may have influenced depression rates, as pre-season depression was assessed prior to classes starting while post-season testing was assessed just before final exams (artificially elevated post-season depression rates). We argue that the combination of school plus demands of training/competition represent a realistic setting for most student-athletes with the expectation of increased depression symptoms within this ecologically valid context. Second, the interval between pre- and post-season testing was likely too long. A midpoint testing assessment would have removed any potential bias of final exams but proved financially and logistically problematic. Third, we did not assess dietary intake nor control for supplement intake, which may have influenced both vitamin and ferritin levels. Lastly, we did not assess or track menstrual history or PMS in female participants which may have influenced depression ratings due to either excessive blood losses (contributing to declining ferritin levels) or timing (i.e., completing the CES-D during the follicular versus luteal phase).

The CES-D is a simple tool that can be easily implemented in future NCAA athlete screenings to monitor athlete mental health over time. Although the incidence of depressive symptoms was lower in our cohort compared with previous cohorts of collegiate athletes and non-athletes, depression scores increased across the season. Higher depression scores on the CES-D may suggest early signs of an underlying vitamin D or ferritin deficiency, particularly in female athletes at the end of the semester and warrants further investigation (i.e., randomized control supplement trials) in larger cohorts.

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