Research Article

Training-specific effects on metabolic-inflammatory mediators: GLP-1 and Dectin-1 changes following resistance, continuous, or interval exercise in overweight women

Leila Nouri Ain[1], Valiollah Shahedi[2*], Yaser Kazemzadeh[3], Sanaz Mirzaian Shanjani[3], Sajad Arshadi[4]

Abstract

The purpose of this study was to examine the effects of eight weeks of resistance, continuous endurance, and interval endurance training on Dectin-1 and Glucagon-Like Peptide-1 levels in overweight women. A total of 40 women, aged between 25 and 35 years with a body mass index (BMI) ranging from 25 to 30 kg/m², voluntarily participated in the study. Participants were randomly assigned to one of four groups: resistance training (n = 10), continuous endurance training (n = 10), interval endurance training (n = 10), and a non-training control group (n = 10). The intervention consisted of three exercise sessions per week over an eight-week period, following structured and group-specific training protocols. Results indicated that all three exercise modalities—resistance, continuous endurance, and interval training—significantly altered Dectin-1 and GLP-1 levels compared to the control group ($p < 0.05$). Among the training groups, continuous endurance training elicited the greatest reduction in Dectin-1 levels, followed by interval training and then resistance training. However, post hoc analysis revealed no significant difference between resistance and interval training groups for either biomarker. Similarly, GLP-1 levels increased most prominently in the continuous endurance group, followed by the interval and resistance training groups, again with no significant difference between the latter two. In summary, the findings suggest that all three forms of exercise contributed to favorable changes in Dectin-1 and GLP-1 among overweight women. Nonetheless, the magnitude of these changes appears to be influenced by the type and possibly the intensity of the training stimulus, with continuous endurance training demonstrating the most pronounced effects.

Key Words: Interval endurance training, Continuous endurance training, Resistance training, GLP-1, Dectin-1

1. PhD student in exercise physiology, Department of Exercise Physiology, I.C., Islamic Azad University, Tehran, Iran. 2. Assistant Professor of Exercise Physiology, Department of Physical Education and Sport Sciences, P.C., Islamic Azad University, Tehran, Iran. 3. Assistant Professor of Exercise Physiology, Department of Exercise Physiology, I.C., Islamic Azad University, Tehran, Iran. 4. Associate Professor, Department of Exercise Physiology, Faculty of Sport Sciences, ST.C., Islamic Azad University, Tehran, Iran.

*Author for correspondence: dr.shahedi@iau.ac.ir

L NA: 0000-0002-3731-7402; V SH: 0000-0001-9046-8341; Y K: 0000-0002-2761-6572; S MS: 0000-0002-4834-4975; S A: 0000-0002-7621-9346

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Introduction

Overweight and obesity are conditions in which excessive or abnormal accumulation of fat increases health risks. Depending on the degree, duration, and distribution of excess adipose tissue, these health risks include type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, nonalcoholic fatty liver disease, chronic kidney disease, obstructive sleep apnea, and mood and physical disorders. The prevalence of obesity is increasing worldwide and has unfortunately become an epidemic that can be an indicator of public health and lifestyle disorders.

Obesity and overweight due to increased fat mass are usually associated with increased plasma glucose levels and increased insulin resistance. Research has shown that controlling glucose and glycemic levels can counteract the destructive effects of obesity and overweight. Among the factors affecting glycemic levels is glucagon-like factor-1 (GLP-1). Glucagon-like factor-1, also known as GLP-1, is a 30-amino acid peptide that is produced in the L cells of the intestinal mucosa after a mixed meal and secreted into the bloodstream (Holst JJ 2023, Bell GI et al 2022). In other words, GLP-1 is primarily produced by enteroendocrine L-cells in the gastrointestinal tract that have an endocrine function, controlling glucose metabolism and energy homeostasis by regulating the secretion of pancreatic hormones and is effective in the treatment of obesity, overweight and diabetes. GLP-1 also inhibits inflammation by affecting the immune system and, due to the presence of GLP-1 receptors in several tissues, affects cardiovascular function in health and disease (Drucker DJ 2016). GLP-1 has been shown to improve glycemic control, weight loss, and liver enzymes in obese, overweight, and type 2 diabetic subjects (Lee J et al 2016). GLP-1 has also been shown to reduce oxidative stress (Trevaskis JL et al 2012) and fibrosis (Lee Y-S et al 2007). It is also effective in the treatment of liver diseases. Chronic administration of GLP-1 has been shown to improve insulin sensitivity and reduce hepatic glucose production using the technique of maintaining normal blood glucose levels. Dectin-1 is an innate immune cell receptor involved in various cellular responses such as chronic inflammation, autoimmune diseases, and diabetes. This receptor is highly expressed on monocytes, macrophages, neutrophils, and other immune cells. Impaired function and expression of Dectin-1 is associated with the development of inflammatory diseases. Data from previous studies indicate that Dectin-1 may be an important indicator in the development of insulin resistance and obesity-induced inflammation because Dectin-1 is expressed on macrophages and plays a role in the development of obesity and insulin resistance by modulating their function and phenotype. It has been shown that inhibition of Dectin-1 is associated with improved glucose homeostasis and insulin sensitivity. In addition, macrophages lacking Dectin-1 have anti-inflammatory properties that are associated with improved insulin sensitivity in adipose tissue.

Given the important role of exercise training in health and the prevention and treatment of complications caused by obesity and overweight, especially inflammation and metabolic disorders, it seems to be of great importance to investigate the effects of various exercise training models on inflammatory-metabolic markers, but according to the studies conducted, the data in this regard are very limited. Considering the above, the present study attempts to examine the effect of three types of exercise training: resistance training, continuous endurance training, and interval training on Dectin-1 and GLP-1 indices in overweight women.

Materials and methods

Subjects

The present study is of semi-experimental research methodology and of applied purpose. The statistical population of this study included all overweight women in Tehran's 9th district, from which 40 eligible participants were selected voluntarily and randomly divided into four groups: resistance training group (10 participants), continuous endurance training group (10 participants), interval endurance training group (10 participants), and control group (10 participants). The study protocol conformed to the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Islamic Azad University Parand Tehran Branch (Ethical code IR.IAU.PIAU.REC.1403.032). In this study, a written consent form was first obtained from the subject stating their full consent to conduct the present study. Then, a specialist physician performed the necessary examinations to ensure that the subjects had no specific problems in order to participate in the study. Then, the anthropometric characteristics of the subjects were evaluated using a body composition measuring device. During one session, all subjects were familiarized with the training protocol methods and how to implement it during 8 weeks. 24 hours before the start of the protocol and also 24 to 48 hours after the end of the 8-week protocol, blood samples were taken to the pathology laboratory to evaluate the indicators under study, and all evaluations were performed using the ELISA method and special kits for measuring each indicator. It should be noted that the entry and exit criteria for the subjects were as follows: they must be overweight, that is, have a body mass index of 25 to 30, there must be no specific disease that makes the subject unable to perform the test, there must be no orthopedic problems that prevent the subject from performing the protocol, they must not have taken any medication or supplement that may have effects on the results, all subjects were female and in the range of 30 to 40 years, and they did not consume tobacco or alcohol. To minimize confounding, subjects were instructed to maintain their habitual diet throughout the study. No formal dietary assessment or control was implemented. Blood samples (10 mL) were collected from the brachial vein after a 12-hour overnight fast at 8:00 AM for both pre-test and post-test assessments. Pre-test samples were obtained 24 hours before the intervention began. Post-test samples were collected 48 hours after the final training session to avoid acute exercise effects. Samples were immediately processed by centrifugation at 3,500–3,800 rpm and stored at -80°C until analysis.

Exercise training protocol

Continuous endurance training

The endurance training protocol was adapted from the Ciolac et al. 2010 and Robbert et al. 2002 training protocols, which started with 55% of maximum heart rate in the first and second weeks and increased by 5% every two weeks to reach 70% of maximum heart rate in the eighth week. The training sessions were conducted three times a week, each session lasting 25 to 45 minutes, from the first to the eighth week. In the first two weeks, the total duration of the subjects' activity was 25 to 30 minutes, and 5 minutes were added to this duration every two weeks, which ultimately reached 40 to 45 minutes in the eighth week. Running activity was performed on a treadmill and heart rate was monitored with a smartwatch. (Ciolac EG et al. 2010, Robbert A 2002).

MHR=208-(0.7 × age).

Interval endurance training

To perform 8 weeks of interval endurance training, the subjects first performed a 10-minute warm-up program that included slow running with stretching exercises, and then a training program that included 6 repetitions of running for a total of 25 to 45 minutes from the first to the eighth week, and the intensity of these exercises was increased from 60 to 75% of maximum heart rate during the 8-week protocol from the first to the eighth week. The rest period between each activity was 1 to 3 minutes in the form of walking and stretching exercises. (It should be noted that the duration of interval training was similar to continuous aerobic trai-

-ning that is isocaloric exercises, but because interval training was accompanied by rest between sets, the intensity was increased by 5% each week with an increase in the number of intervals).

Resistance training

To perform resistance training, first the subjects' one repetition maximum (RM) was assessed using the Berezik formula. Then, the modified resistance training protocol was performed by the subjects as follows (Nasimto et al., 2007, N.C. Nair et al., 2011). First, the subjects warmed up for 10 minutes using machines and at the end of the training session, they also performed a 10-minute cool-down. Weeks one to four: three sets of 15, 20 repetitions at 65% of 1RM, and weeks five to eight: 8 to 12 repetitions at 75% of 1RM. (It should be noted that the duration of resistance training was similar to continuous aerobic and interval training, which are isocaloric exercises, but because resistance training, like interval training, was accompanied by rest between sets, the intensity increase rate was applied by 5% each week) (See details in Table 1).

Biochemical analysis of variables

To evaluate Dectin-1, an ELISA kit and DOUBLE SANDWICH method manufactured by Eastbiopharma Company (EASTBIOPHAR), manufactured in China under a US license (sensitivity 0.78 pg/ml) were used. GLP-1, particularly the active form (GLP-1 (7–36) amide), is highly unstable and rapidly degraded in vivo and ex vivo by the enzyme dipeptidyl peptidase-4 (DPP-4), with a half-life of approximately 1–2 minutes in circulation. Therefore, meticulous sample handling and processing procedures are essential for valid and reproducible. For GLP-1 evaluation, ELISA kit and DOUBLE SANDWICH method manufactured by Eastbiopharma Company (EASTBIOPHAR) manufactured in China under license from the United States (sensitivity 1.26 pg/ml) were used.

Table 1: Resistance training protocol

Goal	Description
Training duration	8 weeks
Training duration per session	25 to 45 minutes
Repetition of training per week	Three sessions
Training intensity	60 to 75% of 1 rep max
Number of repetitions	5 to 20 reps
Number of sets	Three sets
Rest period between sets and each exercise	1-3 minutes
Training exercises	Machine squat, machine leg press, machine front row, machine leg curl, machine back row, machine chest press, cable row, machine biceps curl, machine biceps curl and machine shoulder press

Statistical analysis

Analysis of covariance (ANCOVA) was performed using pre-test values as the covariate to compare post-test means between groups. Tukey's HSD post hoc test was used for pairwise comparisons where ANCOVA indicated significance. Significance was set at $p < 0.05$.

Results

In order to investigate the effect of resistance, continuous endurance and interval training on GLP-1 indices in overweight women, an analysis of covariance was performed. The results obtained from the analysis of covariance test with a significance level of less than 0.05 showed that there was a significant difference between the GLP-1 variable in the three research groups ($P = 0.001$); as a result, the four resistance training methods, continuous aerobic and interval aerobic, had a significant effect on the GLP-1 index in overweight women (Figure 1A). The results of the Tukey post-test showed that the values of dectin-1 in the resistance training, continuous aerobic and interval aerobic groups had a significant increase in the post-test compared to the control group. And this increase was greater in the continuous group than in the other groups.

In order to investigate the effect of resistance, continuous endurance and interval training on Dectin-1 indices in overweight women, an analysis of covariance was performed. The results obtained from the analysis of covariance test with a significance level of less than 0.05 showed that there was a significant difference between the Dectin-1 variable in the four research groups ($P = 0.001$); as a result, the three methods of resistance training, continuous aerobic and interval aerobic training had a significant effect on the Dectin-1 index in overweight women (Figure 1B). The results of the Tukey post-test showed that the values of Dectin-1 in the resistance training, continuous aerobic and interval aerobic training groups had a significant decrease compared to the control group at the post-test. And this decrease was greater in the continuous group than in the other groups.

Discussion

Regarding GLP-1 changes, the present study showed that continuous aerobic exercise significantly increased GLP-1 levels compared to other groups, followed by interval aerobic exercise and finally resistance exercise. Consistent with the findings of the present study, an increase in GLP-1 levels was observed after five days of aerobic exercise in both overweight and normal-weight adolescents (Chanoine JP et al 2008). It has also been shown that a single session of physical activity significantly increased GLP-1 and reduced hunger in obese and non-obese young subjects (Ueda SY et al 2009). The increase in GLP-1 following physical activity was significantly and negatively

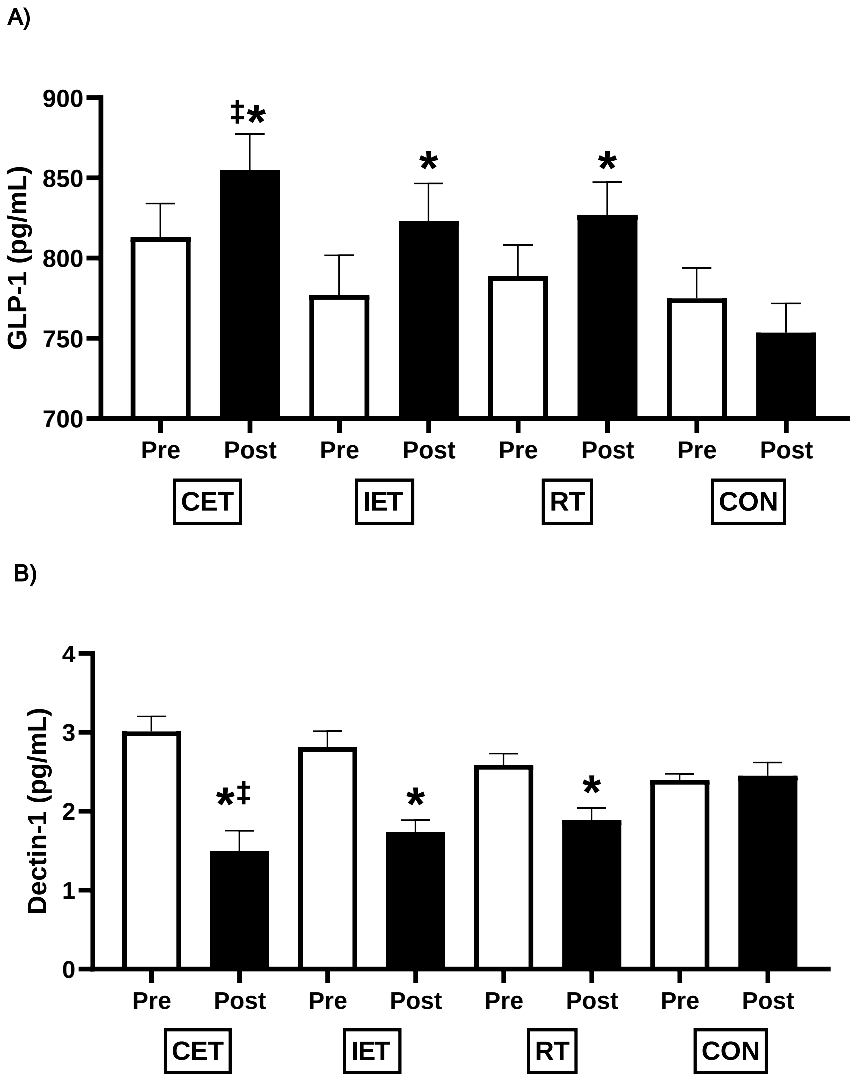

Figure 1. Pre- and post-intervention levels of (A) GLP-1 and (B) Dectin-1 in overweight women following 8 weeks of continuous endurance training (CET), interval endurance training (IET), resistance training (RT), or control (CON). Data presented as Mean ± SEM. * $p < 0.05$ vs. Pre-test within group; † $p < 0.05$ vs. CON post-test; ‡ $p < 0.05$ CET vs. RT and IET post-test. *

associated with energy intake. It has been reported that one hour of cycling at 65% of maximum heart rate increased GLP-1 and, consequently, decreased hunger in young men and women of normal weight (Martins C et al 2007). The results of studies indicate that, considering the intensity of exercise, GLP-1 increases between 50 and 75% of maximum oxygen consumption (Ueda SY et al 2009). These findings suggest that physical activity may regulate GLP-1 release and metabolism, leading to appetite control. However, the physiological mechanisms underlying the exercise-induced increase in GLP-1 remain incompletely understood. Recent evidence points toward a dual neural and humoral pathway: afferent neural signals from contracting skeletal muscles, possibly mediated by the sciatic nerve, may stimulate enteroendocrine L-cells in the gut to secrete GLP-1. In parallel, muscle-derived interleukin-6 (IL-6), released in response to exercise, has been shown to enhance GLP-1 secretion through a humoral pathway, linking skeletal muscle activity directly with gut hormone release (Ellingsgaard H et al 2011). These pathways may act synergistically or independently depending on exercise modality, intensity, and duration.

However, the results of the present study are inconsistent with the findings of some studies (Martins C et al 2010, Kullman EL et al 2016). Thus, Coleman et al. (2016) observed a decrease in GLP-1 levels in obese subjects with non-alcoholic fatty liver disease after a 7-day training period at 85% of maximum heart rate. Martins et al. (2010) also observed in a study that 12 weeks of training program (5 days a week at 75% of maximum heart rate) leads to a significant reduction in body weight without significant changes in fasting GLP-1 levels. However, they observed that postprandial GLP-1 levels were slightly higher in obese or overweight men and women after 12 weeks of training (Martins C et al 2010). The reason for the different findings is probably the difference in the exercise protocol including duration, type and intensity of exercise. Also, the difference in the fitness and training status of the subjects is important. Baseline metabolic health—such as obesity, insulin resistance, or fatty liver disease—can modulate the GLP-1 response to exercise. For example, chronic inflammation and altered gut hormone dynamics in metabolic disorders may blunt the exercise-induced rise in GLP-1. Furthermore, nutritional status, timing of measurements (fasting vs. postprandial), and individual variability in gut microbiota may all contribute to the heterogeneity in findings across studies.

Although exercise leads to an increase in plasma GLP-1 levels, the physiological mechanisms for this phenomenon are still not fully elucidated, as highlighted above. The increase in plasma GLP-1 levels during exercise may indeed be mediated by afferent pathways of the sciatic nerve. Recently, it has been shown that this increase is also mediated by interleukin-6 distributed from skeletal muscle through a humoral pathway (Ellingsgaard H et al 2011). Further studies are needed to clarify the relative contribution and potential interaction between these neural and humoral mechanisms for increasing plasma GLP-1 levels following exercise.

Also, the results of the present study showed that the resistance training group had a significant increase in GLP-1 compared to the control group. Contrary to the results of the present study, Shaabani M et al (2016) investigated changes in serum GLP-1 in women with type 2 diabetes following four weeks of exercise training. They stated that performing exercises (five times a week, for four weeks at 55 to 80% of maximum heart rate) had no effect on serum GLP-1, glucose, and insulin levels in women with type 2 diabetes. Among the reasons for the differences between the results of Shaabani et al.'s study and the results of the present study can be attributed to the frequency, intensity, and duration of the exercise protocol; because it seems that increasing the intensity and volume of exercise play a significant role in increasing GLP-1. Additionally, population characteristics—such as diabetes status, degree of metabolic dysfunction, and medication use—may further influence hormonal responses to exercise. In this regard, Lee et al (Lee SS et al 2015) investigated the effect of interval training (walking and running 30 × 30 seconds on a treadmill, three times a week, for 12 weeks at 80% of heart rate reserve and moderate-intensity aerobic training, treadmill training, six times a week, for 12 weeks at 40% of heart rate reserve) on serum GLP-1 levels in people with diabetes. They stated that high-intensity interval training had better effects on serum GLP-1 levels, glycemic indices, and body composition in patients with type 2 diabetes. This suggests that exercise intensity, modality, and patient characteristics all interact to determine the GLP-1 response.

The results of the present study showed that various exercise trainings have different effects on dectin-1 levels, and these changes are significant among groups. By and large, continuous aerobic training causes the greatest reduction compared to interval and resistance training, as well as control. Regarding the changes in dectin-1, it should be noted that dectin-1, a C-type lectin receptor involved in innate immunity, can also be regulated by various cytokines such as IL-4 and GM-CSF, as well as by microbial components (Reid et al., 2004). The response of dectin-1 to exercise and the mechanisms of changes in dectin-1 levels following exercise are not known. However, it is possible that continuous aerobic exercise, which had the greatest reducing effect on dectin, led to changes in dectin-1 protein through its effect on IL-4 and GM-CSF levels. However, the above factors were not examined in the present study, which is a limitation of this study. Dectin-1 also requires interferon regulatory factor (IRF) for immune response, and IRF is essential for the differentiation of AT1M macrophages, which play a major role in obesity-induced insulin resistance (del Fresno et al., 2013; Krausgruber et al., 2011). In addition, it has been reported that Dectin-1 is activated by vimentin expressed in mesenchymal cells (Thiagarajan et al., 2013). Therefore, it is likely that the effects of exercise on changes in Dectin-1 are mediated by vimentin—potentially through modulation of extracellular matrix dynamics or immune cell activity—but this remains speculative. However, further studies are needed in this area. It seems that the difference between previous studies and the above findings is due to the type of subjects studied. The contradiction in the results of the studies can be due to different factors such as the type of nutrition, exercise program, type of subject and duration of exercise. For example, Ruffino et al. reported that after 8 weeks of moderate-intensity exercise program (walking, three times a week), Dectin-1 increased significantly in sedentary women. The difference between the above results and the findings of this study can be attributed to the difference between the type of protocol and the duration of exercise. Acute versus chronic exercise, the presence of underlying inflammation, and the balance between pro- and anti-inflammatory cytokines in the tissue microenvironment may all shape the dectin-1 response.

Conclusion

In summary, while dectin-1 is responsive to exercise, the underlying mechanisms—including potential roles of cytokines (IL-4, GM-CSF), transcription factors (IRF), and extracellular matrix proteins (vimentin)—warrant further mechanistic investigation, especially in relation to metabolic and immune health.

What is already known on this subject?

Obesity and overweight due to increased fat mass are usually associated with increased plasma glucose levels and increased insulin resistance.

What this study adds?

The present study showed that different training methods have significant effects on each of the GLP-1 and dectin-1 indices in overweight women. Tukey's post hoc test showed that continuous aerobic training had the greatest increasing effect on GLP-1 compared to other groups, followed by interval training and finally resistance training, which had greater increasing effects, but this effect was not significant between resistance and interval training. Also, continuous aerobic training had the greatest decreasing effect on dectin-1 compared to other groups, followed by interval training and finally resistance training, which had decreasing effects, but this effect was not significant between resistance and interval training. In general, it can be concluded that the type of training can have different and significant effects on each of the inflammatory-metabolic indices.

Organ Cross-Talk Tips:

- Exercise training, particularly continuous endurance, significantly elevated gut hormone GLP-1 levels, indicating muscle-derived signals impact metabolic/enteroendocrine function.
- Continuous endurance training induced the strongest Dectin-1 reduction and GLP-1 elevation, highlighting how exercise type/intensity differentially regulates organ communication magnitude.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval the study protocol conformed to the Declaration of Helsinki and was approved by the animal care and use committee of Islamic Azad University parand Tehran branch (Ethical code IR.IAU.PIAU.REC.1403.032).

Informed consent Participants signed an informed consent form prior to participation in the study.

Author contributions

Conceptualization: L.N.A, V.SH,; Methodology: L.N.A, V.SH, Y.K, S.M.S, S.A,; Software: L.N.A, V.SH, Y.K, S.M.S, S.A,; Validation: L.N.A, V.SH, Y.K, S.M.S, S.A,; Formal analysis: L.N.A, V.SH, Y.K, S.M.S, S.A,; Investigation: L.N.A, V.SH, Y.K, S.M.S, S.A,; Resources: L.N.A, V.SH, Y.K, S.M.S, S.A,; Data curation: L.N.A, V.SH, Y.K, S.M.S, S.A,; Writing - original draft: L.N.A, V.SH, Y.K, S.M.S, S.A,; Writing - review & editing L.N.A, V.SH, Y.K, S.M.S, S.A,; Visualization: L.N.A, V.SH, Y.K, S.M.S, S.A,; Supervision: L.N.A, V.SH, Y.K, S.M.S, S.A,; Project administration: L.N.A, V.SH, Y.K, S.M.S, S.A,; Funding acquisition: L.N.A, V.SH, Y.K, S.M.S, S.A.

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