Research Article

Differential changes in serum levels of transforming growth factor beta and interleukin-17 ratio in overweight pregnant women and their fetuses after home-based exercise training

Mahdieh Molanuri Shamsi[1,2*], Lida Moghaddam-Banaem[3], Marzieh Moslemi[1], Farzaneh Sinapour[1], Mona Pourmohammad[3], Afsaneh Jamali[1], Raoof Negaresh[4], Sara Soudi[5], Katsuhiko Suzuki[6]

Abstract

This study investigates the effect of home-based combined exercise on the transforming growth factor-β/Interleukin-17 ratio (TGF-β/IL-17) in maternal serum during the first, second, and third trimesters of pregnancy, as well as in umbilical cord blood. Thirty overweight pregnant women were randomly allocated to control and training groups. Blood samples were collected during each trimester of pregnancy and from the umbilical cord at birth. Fitness-related indicators were assessed in the mother throughout pregnancy. Newborn health indicators were measured at birth. The levels of IL-17 and TGF-β were determined using enzyme-linked immunosorbent assay (ELISA) and specialized kits. The exercise training significantly reduced TGF-β levels ($p=0.011$, effect size=1.22) and the TGF-β/IL-17 ratio ($p=0.045$, effect size=0.79) in the third trimester in mothers. Similarly, this ratio decreased in the fetus, accompanied by an increase in IL-17 levels ($p = 0.038$, effect size = 0.93). These immune changes were associated with improved maternal cardiovascular fitness and higher Apgar scores at 5 minutes for newborns ($p<0.05$). Obesity and excessive weight gain during pregnancy are linked to inflammatory responses and elevated cytokine levels, which may increase the risk of complications for the mother. This study highlights the long-term benefits of maternal exercise, evidenced by reduced inflammatory responses and improved neonatal health outcomes, as reflected in Apgar scores.

Key Words: **Pregnancy, Overweight, Cytokines, Home-based exercise, Neonatal outcomes**

Introduction

The global prevalence of obesity and overweight is a significant public health concern, with particular attention being paid to its rise among women of childbearing age in recent years. Obesity during pregnancy is associated with numerous adverse maternal and fetal outcomes, including an increased risk of complications that can disrupt normal pregnancy progression (Santos et al., 2019; Shin & Song, 2015). Specifically, obesity has been linked to alterations in immune system indicators and inflammatory responses, which are crucial during pregnancy (Bernhardt et al., 2022; Hekmatikar, Shamsi, Ashkazari, & Suzuki, 2021; Li et al., 2021).

Pregnancy involves distinct inflammatory environments across its different stages. The first and third trimesters are characterized by a pro-inflammatory state, while the second trimester is predominantly anti-inflammatory (Mor, Cardenas, Abrahams, & Guller, 2011). A healthy pregnancy requires a carefully balanced and regulated inflammatory environment, but obesity during pregnancy can disrupt this balance, potentially leading to adverse outcomes for both the mother and fetus (Bodnar, Ness, Harger, & Roberts, 2005; Hauguel-de Mouzon & Guerre-Millo, 2006).

One of the key regulatory factors in immune system modulation is transforming growth factor-Beta (TGF-β). TGF-β plays a critical role in regulating immune responses in leukocytes and vascular endothelial cells. Despite its regulatory functions, elevated levels of TGF-β have been implicated in the pathogenesis of various conditions, including renal and cardiovascular diseases (Muy-Rivera et al., 2004; Topper, 2000). Elevated plasma TGF-β concentrations have also been suggested as predictors of preeclampsia, a hypertensive disorder of pregnancy characterized by chronic systemic inflammation, endothelial dysfunction, renal impairment, and hypertension (Djurovic et al., 1997; Muy-Rivera et al., 2004).

Additionally, the imbalance between different T cell populations, particularly the balance between Th1 and Th2 cells, has traditi-

1. Department of Physical Education & Sport Sciences, Faculty of Humanities, Tarbiat Modares University, Tehran, Iran. 2. Department of Physical Education & Sport Sciences, Yazd University, Yazd, Iran. 3. Department of Reproductive Health and Midwifery, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran. 4. Department of Physical Education, Farhangian University; P.O. Box 14665-889, Tehran, Iran. 5. Department of Immunology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran. 6. Faculty of Sport Sciences, Waseda University, Tokorozawa, Japan.

*Author for correspondence: molanouri@modares.ac.ir

M M S: 0000-0003-4665-5363; L M B: 0000-0002-9849-7451; M M: 0000-0002-0379-3603; F S: 0000-0001-6509-0332; M P: 0000-0003-0980-1181; A J: 0000-0003-2097-2651; R N: 0000-0003-4686-4130; S S: 0000-0002-8978-3958; K S: 0000-0002-6572-5809

Received 8 October 2024; Accepted 13 December 2024

-onally been considered important in pregnancy outcomes (Saito, Tsuda, & Nakashima, 2023). However, recent studies have highlighted the role of T helper 17 (Th17) cells and the systemic cytokine interleukin-17 (IL-17) in the pathogenesis of various diseases, including pregnancy-related complications (Osborne, Brar, & Klein, 2019; Tang & Hu, 2023). The interplay between T regulatory cells, cytokines such as TGF-β, and the Th17/IL-17 axis in overweight pregnant women remains underexplored.

Moreover, changes in immune responses observed in umbilical cord blood may provide insights into the future immune function of the newborn (Zhang, Guan, & Zhong, 2023). Some studies have suggested that physical activity can modulate cytokine responses in umbilical cord blood (Acosta-Manzano et al., 2019; Moroishi et al., 2023). However, the specific impact of different types of physical activity on cytokines such as IL-17 and TGF-β remains unclear.

Regular physical activity has been recognized for its role in managing pregnancy-related complications. Even without significant changes in body weight, physical exercise during pregnancy has been shown to improve quality of life, physical fitness, and reduce the risk of complicated pregnancies (Kubler, Clifton, Moholdt, & Beetham, 2022). Home-based exercise programs have gained attention in recent years due to various barriers to traditional exercise, such as lack of time, childcare responsibilities, fatigue, cost, limited access to exercise facilities, and public health concerns such as infectious disease outbreaks (Chaabene et al., 2021; Mokhtarzade et al., 2021). Although some studies have examined the effects of combined exercise training on improving immune system markers in pregnant women, few studies have investigated the combination of combined home-based exercise training in overweight pregnant women.

Given the potential relationship between immune system indicators, particularly cytokines, and maternal and fetal health in overweight and obese women, this study aims to investigate the effects of home-based exercise training during the second and third trimesters of pregnancy. The study focuses on maternal and fetal serum levels of IL-17, TGF-β, and the TGF-β/IL-17 ratio, as well as physical fitness-related indices including cardiovascular fitness, body composition, and musculoskeletal fitness in pregnant women.

Materials and Methods

Ethic and subjects

Blood samples used in this study were obtained from participants of a previous clinical trial (IRCT20190410043222N1). This interventional, randomized clinical trial utilized convenience sam-

-pling, targeting overweight pregnant women aged 18–37 years with a pre-pregnancy BMI of 25–29.9 kg/m² or within the first 12 weeks of gestation. Participants were enrolled between the 16th and 18th week of pregnancy, with eligibility criteria including Iranian nationality and no contraindications to physical activity, as per guidelines by the American College of Obstetricians and Gynecologists and Canadian physical activity guidelines.

Sample size was determined using G*Power software, requiring 30 participants to achieve 95% power and 5% Types I error. Participants were randomly assigned to a training group (n=15) or a control group (n=15). The study spanned from the 16th–18th week of pregnancy to delivery. Maternal blood samples were collected at the 16th–18th, 25th–29th, and 36th–37th weeks, while umbilical cord blood samples were obtained at delivery. Neonatal metrics (weight, height, thoracic and head circumferences, and Apgar scores at 1 and 5 minutes) were also recorded.

The study was approved by Tarbiat Modares University's Ethics Committee. Participants provided written informed consent after receiving detailed information on the study's objectives, procedures, and potential benefits. They were free to withdraw at any time.

Measurements

Anthropometrics: Height and weight were measured using a stadiometer and a calibrated digital scale (Seca, Germany), with accuracies of 0.1 cm and 0.1 kg, respectively. BMI was calculated, and body fat percentage was estimated using the three-site skinfold method with a Harpendent caliper. Waist-to-hip ratio (WHR) was derived from circumference measurements.

Physical Fitness: Muscular strength and endurance were assessed using a Jamar dynamometer. Strength was measured by recording the average of three maximum-effort squeezes, while endurance was assessed by measuring the duration of holding the dynamometer at 30% of maximum voluntary contraction (Baffour-Awuah, Pearson, Dieberg, Wiles, & Smart, 2023). Cardiovascular endurance was evaluated with the 6-minute walk test, a validated method for pregnant women (Dennis et al., 2019).

Blood Sampling and Analysis: Maternal blood samples (8 mL) were drawn after a 12-hour fast under controlled conditions, centrifuged at 3000 RPM for 15 minutes, and serum was stored at -20°C. IL-17 and TGF-β cytokine levels were analyzed using ELISA kits (R&D Systems) per manufacturer instructions.

Intervention

The training group followed a structured program of aerobic and resistance training, starting from the 16th–18th week until the 36

th–37th week, totaling 95–110 sessions. Aerobic exercises (e.g., walking) were performed thrice weekly, with resistance training targeting major muscle groups twice weekly. Each session included a 10-minute warm-up and cool-down with stretching. Exercise intensity was monitored using the Borg rating of perceived exertion (RPE) scale and the talk test. Participants were educated on hydration, nutrition, and warning signs requiring medical attention.

Adherence was monitored through weekly phone calls and virtual check-ins. Participants submitted exercise reports, and in-person re-training sessions were available when needed. The control group received standard prenatal care without specific exercise recommendations (Artal & O'Toole, 2003; Cilar Budler & Budler, 2022; "Physical Activity and Exercise during Pregnancy and the Postpartum Period: ACOG Committee Opinion, Number 804," 2020).

Statistical analysis

Data analysis was performed using SPSS 21. Two-way analysis of valiance (ANOVA) with repeated measures and two-way ANOVA were used for comparisons between groups (exercise vs. control) and across time points. Partial eta squared ($p\eta^2$) was reported as the effect size. T-tests were conducted for changes relative to the first trimester, with Cohen's test used for effect size estimation. A significance level of 0.05 was applied.

Results

Participants

Out of the 30 participants, 25 completed the study, resulting in a completion rate of 83.3%. Two participants from the training group and three from the control group were excluded. The exclusions in the control group were due to a lack of willingness

Table 1. Aerobic and resistance exercise protocol.

Pregnancy weeks	Aerobic Exercise Training			Resistance Exercise Training				
	Session per Week	Session Duration (min)	RPE[a]	Session per Week	Type of exercise	Set	Repetition	Rest between sets (min)
16-17	3	15	12-14	2	6	2	10-11	1
18-21	3	20	12-14	2	9	2	12-15	1-2
22-26	3	25	12-14	2	9	2	15	2
27-30	3	30	12-14	29	9	2	12	2
31-35	3	30	12-14	2	7	2	10	1-2
36-40	3	30	12-14	2	7	2	10	1-2

a: Rating of perceived exertion

Table 2. Demographic characteristics of participants and pregnancy details.

		Exercise	Control
Age (year)		30.7±3.8	30.7±4.3
1st trimester Weight (kg)		70.5±4.1	69.7±5.7
2nd trimester Weight (kg)		80.9±5	78.1±7.6
3rd trimester Weight (kg)		85.1±6.5	82.5±8
1st trimester BMI (kg/m2)		27.1±1	27.3±1.7
2nd trimester BMI (kg/m2)		31.1±1.1	30.6±2.4
3rd trimester BMI (kg/m2)		32.4±0.9	32.1±2.4
Employed	Yes	3 (25%)	4 (44%)
	No	9 (75%)	5 (54%)
Education	Below the bachelor's degree	1 (8%)	1 (11%)
	Bachelor's degree or higher	11 (92%)	8 (89%)
Family relationship	Yes	2 (17%)	0 (0%)
	No	10 (83%)	9 (100%)
Physical activity before pregnancy	No regular activity	3 (25%)	1 (11%)
	light regular activity	9 (75%)	8 (89%)
Gender of the fetus	Boy	9 (75%)	6 (67%)
	Girl	3 (25%)	3 (33%)
Delivery	Vaginal	1 (8%)	1 (11%)
	Cesarean	11 (92%)	8 (89%)

BMI: body mass index

to continue with the study, while in the training group, the reason was the expiration of health insurance coverage at the center where the study was conducted.

Feedback was continuously collected throughout the study, and no side effects, such as joint pain or muscle soreness, were reported from the exercises. However, body contusion was a common report among participants during the first few weeks. Overall, the exercise program was well-tolerated and effectively completed by the participants in the training group. Adherence to the exercise regimen was 70%, as monitored through weekly phone calls.

The demographic characteristics of participants and pregnancy details are presented in Table 2. At baseline, there were no significant differences between the groups ($p > 0.05$). Additionally, the characteristics of the newborns are shown in Table 3. While there were no significant differences in the Apgar score at 1 minute ($p = 0.65$), height ($p = 0.94$), weight ($p = 0.41$), or head ($p = 0.88$) and thoracic circumferences ($p = 0.40$) of the newborns, the Apgar scores at 5 minutes were significantly higher in the group whose mothers exercised ($p = 0.04$).

IL-17 and TGF-β

The results from the two-way repeated measures ANOVA showed no significant main effects for group, time, or interaction for IL-17 ($p = 0.735$, $p\eta^2 = 0.002$; $p = 0.102$, $p\eta^2 = 0.071$; and $p = 0.999$, $p\eta^2 = 0.001$, respectively) (Figure 1). In contrast, the analysis of TGF-β revealed significant main effects for time and interaction ($p = 0.004$, $p\eta^2 = 0.173$; and $p = 0.028$, $p\eta^2 = 0.118$, respectively), but no significant main effect for the group ($p = 0.028$, $p\eta^2 = 0.118$). The Bonferroni post-hoc test indicated a significant difference between the exercise and control groups during the third trimester ($p=0.01$), as well as within the training group between the first and third trimesters ($p=0.001$). When the TGF-β/IL-17 ratio was analyzed, a significant main effect for time

Table 3. Details of the newborn.

	Exercise	Control
Apgar score 1 min	8.9±0.3	8.5±0.5
Apgar score 5 min	9.6±0.5	*9.1±0.4
Weight (kg)	3.2±0.3	3.3±0.3
Height (cm)	50.1±1.2	50.2±1.7
Head circumference (cm)	34.7±1.5	34.5±2
Thoracic circumference (cm)	33.8±1.3	33.3±1.4

* Indicate significant difference independed t test.

Table 4. Body composition and fitness data in exercise and control groups.

		Time 1	Time 2	3rd-1st trimester weigh (kg)
Weight (kg)	Control	69.7±5.7	82.5±8	12.8±3.7
	Exercise	70.5±4.1	85.1±6.5	14.6±3.3
BMI (kg/m²)	Control	27.3±1.7	32.1±2.4	4.8±1.2
	Exercise	27.1±1	32.4±0.9	5.3±1.19
WHR	Control	0.94±0.02	0.98±0.03	0.03±0.02
	Exercise	0.89±0.05	0.94±0.03	0.04±0.05
BF%	Control	34.52±3.79	41.46±3.61	6.94±2.78
	Exercise	36.20±4.71	42.12±4.69	5.91±3.47
HR (bpm)	Control	96±8.88	102.66±7.61	6.66±14.56
	Exercise	84.66±8.11	93±10.7	8.33±12.78
SBP (mmHg)	Control	94.44±11.3	100±8.66	5.55±10.13
	Exercise	102.08±9.4	105±7.07	2.91±11.95
DBP (mmHg)	Control	61.11±6.01	60±7.07	-1.11±10.54
	Exercise	65±9.04	64.16±7.92	-0.83±13.11
FBS (mg/dl)	Control	84.77±7.96	81±7.71	-3.07±8.54
	Exercise	82.41±8.17	79.41±4.98	-3±7.49
HB (g/dl)	Control	12.84±0.73	11.61±0.81	-1.23±1.23
	Exercise	12.95±0.76	12.18±1.12	-0.77±0.74
MVC (N)	Control	42.95±6.7	37.22±7.91	-5.73±10.01
	Exercise	48.35±15.33	45.43±12.49	-2.91±9.71
MVC30 (s)	Control	135.88±43.37	121±42.76	-14.88±40.11
	Exercise	161.75±34.38	169.83±20.49	8.08±27.03
6WMT (m) *	Control	356.66±30.01	290.95±32.96	-65.70±42.47#
	Exercise	355.5±48.32	370.76±39.18	15.26±45.22

NA: not available; BMI: body mass index; WHR: waist to hip ratio; BF%: body fat percentage; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HB: hemoglobin; FBS: fasting blood sugar; MVC: maximum voluntary contraction; 6MWT: 6-minute walk test. There was no statistical significance.

* Indicate significant difference in 2-way ANOVA test ($p<0.05$). # Indicate significant difference in independed t test ($p<0.05$).

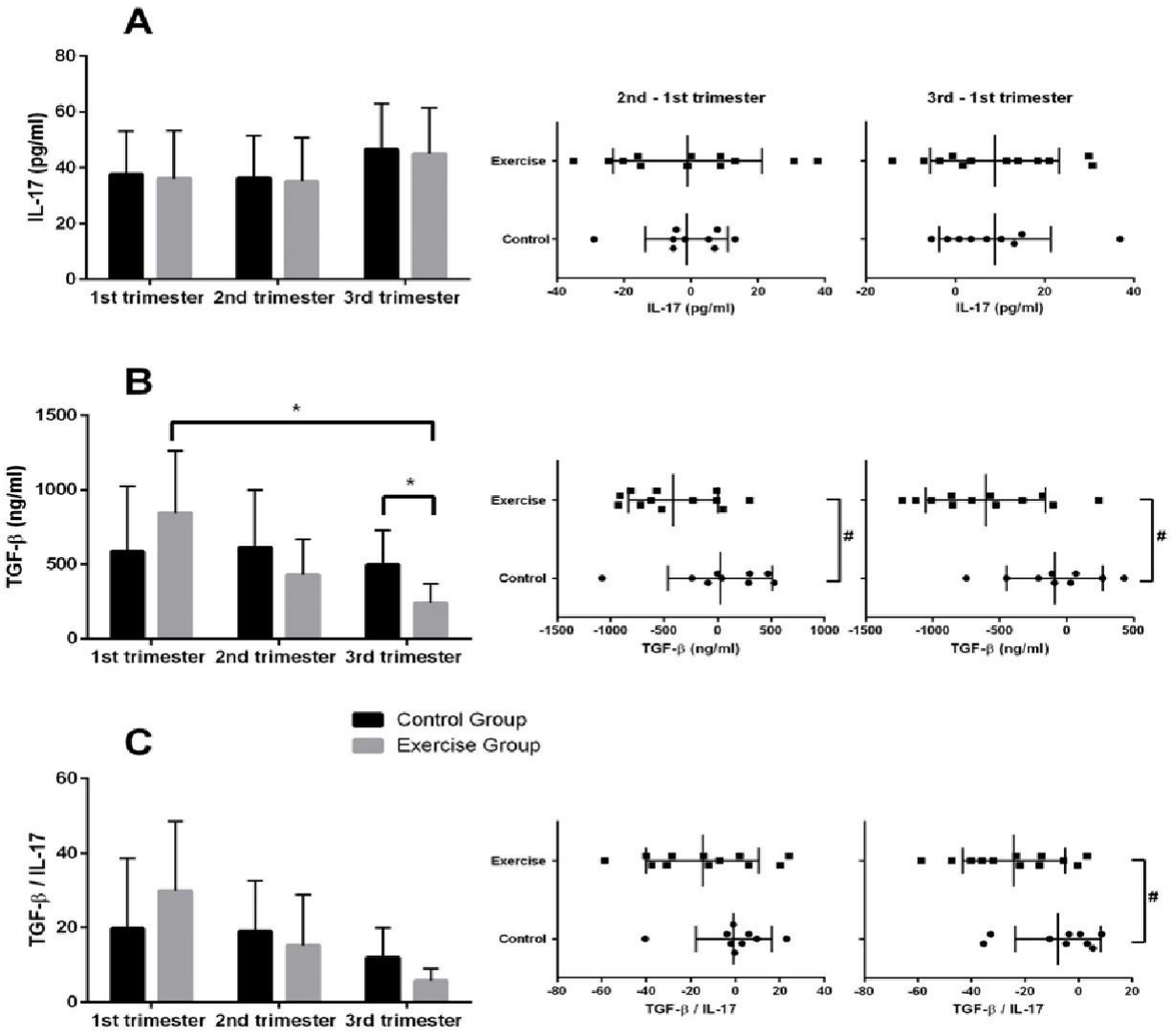

Figure 1. Effect of exercise during pregnancy on IL-17 and TGF-β.

* Indicate significant difference in 2-way repeated measures ANOVA test (p<0.05). # Indicate significant difference in independed t-tests (p<0.05).

was found (p = 0.002, pη² = 0.196), but no significant main effects for the group (p = 0.981, pη² = 0.001) or interaction (p = 0.124, pη² = 0.071) were observed (Figure 1).

Changes in IL-17 levels across trimesters were not significant (p=0.96, ES=0.01 for second trimester and p=0.93, ES=0.01 for third trimester). However, significant changes in TGF-β levels were observed between the first and second trimesters (p = 0.039, ES = 0.96) and between the first and third trimesters (p = 0.011, ES = 1.27). Additionally, the TGF-β/IL-17 ratio showed significant changes in the third trimester compared to the first trimester (p = 0.045, ES = 0.79).

Data extracted from cord blood (Figure 2) indicated significant differences between the exercise and control groups for both IL-17 (p = 0.038, ES = 0.93) and the TGF-β/IL-17 ratio (p = 0.004, ES = 1.39), with the training group showing higher and lower levels, respectively. Although there was a trend toward higher TGF-β levels in the control group compared to the training group, the difference was not statistically significant (p = 0.083, ES = 0.81).

Body composition and fitness

The body composition and physical fitness details are presented in Table 4. The 2-way repeated measure ANOVA for all body composition outcomes include weight (p=0.001, pη2=0.316), BMI (p=0.001, pη2=0.492), WHR (p=0.004, pη2=0.202) and BF% (p=0.001, pη2=0.375) revealed significant main time effect whereas all mentioned outcomes did not have a significant time*group interaction effect (p>0.05). All mentioned outcomes were associated with gradual increase over time. In addition, the

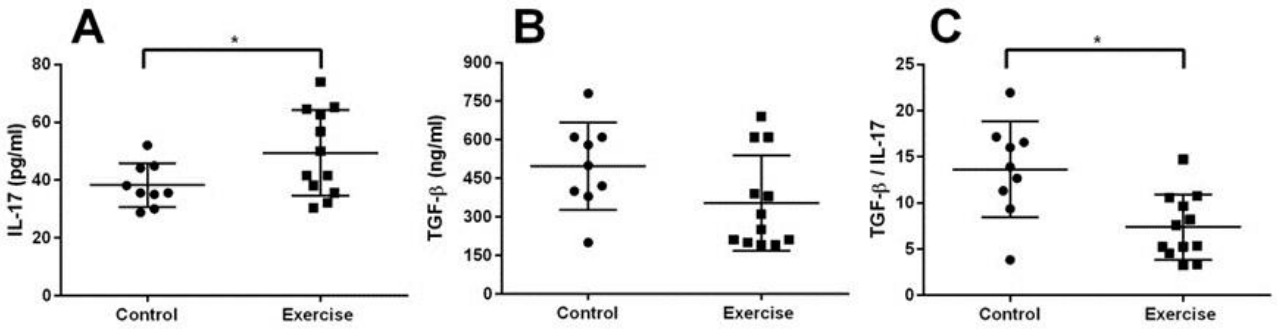

Figure 2. Effect of exercise during pregnancy on IL-17 and TGF-β of cord blood.

* Indicate significant difference independed t-tests (p<0.05).

gradual increase in the outcomes compared to 1st trimester did not indicate a significant difference between the training and control groups (p=0.09-0.81).

Analyzing data on heart rate and blood pressure provided that both resting heart rate (HR) (p=0.001, pη2=0.269) and systolic blood pressure (SBP) (p=0.032, pη2=0.116) were associated with main group effect; however, resting HR also showed main time effect (p=0.011, pη2=0.158) in a way that the increase in the HR of the both groups was noticeable. Diastolic blood pressure (DBP) data did not observe any significant main or interaction effect (p>0.05). Similarly, fasting blood sugar (FBS) results demonstrated no significant changes in the response to intervention; however, hemoglobin (HB) data had only main time effect (p=0.001, pη2=0.257).

Finally, the current physical fitness outcomes include MVC and MVC30 did not indicate any significant main time or interaction effect (p>0.05); nevertheless, MVC30 (p=0.002, pη2=0.233) data were accompanied just by a significant main group effect. As with the previous results, when the difference between the two measurement times was calculated, there was no significant difference between the training vs. control groups in MVC and MVC30 (p>0.05). The results of 6MWT indicate significant main time (p=0.046, pη2=0.101), group (p=0.003, pη2=0.214) and interaction effect (p=0.002, pη2=0.224). Bonferroni's post hoc test showed that at 3rd trimester, 6WMT records of the training group was significantly higher (p=0.001). Additionally, analyzing amount of changes in 6WMT records over the time indicates significant difference (p=0.012) (Table 4).

Discussion

This study investigates the impact of home-based exercise training in overweight women during early pregnancy on maternal and neonatal health indicators, focusing on cytokines TGF-β, IL-17, and their ratio. The findings revealed that maternal exercise training reduced TGF-β levels and the TGF-β/IL-17 ratio in over-weight mothers during the third trimester. Umbilical cord blood analysis showed increased IL-17 levels in fetuses and a decreased TGF-β/IL-17 ratio. Additionally, improvements were noted in newborn Apgar scores at five minutes and maternal cardiovascular fitness in the training group.

The results demonstrate the beneficial effects of physical activity on maternal and fetal health, even with low-to-moderate intensity exercise routines suitable for home settings. These exercises effectively reduced TGF-β levels and the TGF-β/IL-17 ratio in the third trimester, suggesting a modulation of inflammatory responses. Maternal obesity is linked to heightened inflammatory markers, posing risks during pregnancy (Cirulli, De Simone, Musillo, Ajmone-Cat, & Berry, 2022). TGF-β plays a critical role in immune regulation and tissue repair during pregnancy (Sanjabi, Oh, & Li, 2017). Its reduction indicates a potential improvement in maternal and fetal health through modulated immune responses. Previous research has demonstrated that various types of physical activity, such as aerobic and resistance training, can modulate immune markers, including TGF-β and IL-17, in populations with the metabolic disorders (Gleeson et al., 2011). Similarly, dietary interventions, particularly those rich in anti-inflammatory nutrients like omega-3 fatty acids and polyphenols, have been shown to regulate these cytokines (Calder, 2010).

In the fetus, a decrease in the TGF-β/IL-17 ratio and an increase in IL-17 levels suggest that maternal exercise influences the maternal immune system and transfers these effects to the fetus. IL-17 plays a role in adaptive immunity, potentially preparing the neonatal immune system for postnatal challenges (Pieren, Boer, & de Wit, 2022). Similar findings have been reported in studies linking maternal physical activity to enhanced neonatal immune function and reduced disease risks later in life (Gascoigne et al., 2023; Lawrence, Ruoss, & Wynn, 2018). However, further research on immune markers and inflammation is necessary to validate these findings.

Interestingly, the exercise program did not lead to significant cha-

-nges in maternal weight or body composition. However, it maintained musculoskeletal fitness and improved cardiovascular fitness, as shown by the 6-minute walk test. Previous studies in non-pregnant individuals' attribute changes in cytokines to fat mass reduction, but in pregnancy, cytokine dynamics differ across trimesters (Spence et al., 2021). Improved cardiovascular fitness may contribute to reduced inflammatory responses during the third trimester, aligning with studies linking fitness to lower inflammation and disease risks (González-Gil et al., 2022).

Enhanced cardiovascular fitness has broader implications for maternal health, improving the ability to manage pregnancy demands and delivery. It may also help prevent conditions like hypertension and preeclampsia, which are common in overweight pregnancies (Witvrouwen, Mannaerts, Van Berendoncks, Jacquemyn, & Van Craenenbroeck, 2020). Notably, improvements in maternal fitness coincided with better neonatal outcomes, including higher 5-minute Apgar scores, which assess newborn health based on heart rate, respiratory function, reflexes, and muscle tone (Apgar, 1953).

Improved fitness and cytokine modulation likely contributed to better placental blood flow and reduced maternal stress during labor, positively impacting neonatal health. Maternal exercise has also been associated with long-term benefits for children, including better cognitive function and reduced metabolic disease risks (Guinhouya, Duclos, Enea, & Storme, 2022). These potential links merit further investigation through long-term studies of child development.

Moreover, the lack of significant changes in maternal weight or body composition despite improvements in inflammatory markers warrants further exploration. One possible explanation is that exercise-induced benefits on inflammation may occur independently of substantial weight loss, as physical activity can enhance metabolic health through mechanisms such as improved insulin sensitivity, mitochondrial function, and cytokine regulation (Amani Shalamzari, Agha Alinejad, Gharakhanlou, Molanouri Shamsi, & Talebi Badrabadi, 2009; Gleeson et al., 2011). Additionally, exercise has been shown to promote favorable shifts in body composition, such as increased muscle mass and reduced visceral fat, even when overall weight remains stable (Mahdieh et al., 2023; Ross et al., 2000). Furthermore, pregnancy-related hormonal and metabolic adaptations, including fluid retention and changes in fat distribution, may have masked measurable reductions in weight or body composition (Catalano & Shankar, 2017). Expanding on these factors would provide a more comprehensive interpretation of the findings and highlight the potential for exercise to confer health benefits beyond weight loss.

This study highlights the advantages of home-based exercise, offering flexibility and eliminating the need for gym access, which is particularly beneficial for pregnant women with time constraints or discomfort exercising in public. Weekly monitoring and motivational strategies in this study ensured high adherence to the exercise program. However, challenges remain, including maintaining motivation, ensuring safety, and addressing the lack of specialized supervision. Combining exercise with nutritional interventions could enhance outcomes by effectively addressing body composition changes.

One limitation of this study is the small sample size, as it included only overweight pregnant women from Tehran. Future studies should aim to include larger sample sizes and more diverse populations to enhance the generalizability of the findings. Additionally, due to the challenges of accessing participants beyond three months of pregnancy, adherence to the exercise program was approximately 70%. Another limitation is the lack of dietary control, which may have influenced the outcomes. Future research could explore a combination of home-based exercises and supervised training while also incorporating dietary monitoring to better assess immunological markers and improve adherence rates.

Conclusion

This study underscores the benefits of home-based exercise for overweight and obese pregnant women, particularly in reducing inflammatory responses and improving cardiovascular fitness. These improvements might positively influence maternal and neonatal health, emphasizing the potential of home-based exercise as a convenient and flexible approach. Future research should explore integrating lifestyle interventions, including exercise and nutrition, to optimize health outcomes for mother and child. Long-term studies are also necessary to evaluate the sustained effects of maternal exercise during pregnancy on child health and development.

What is already known on this subject?

Various studies have confirmed the beneficial effects of physical activity on maternal health and pregnancy-related complications in both the mother and fetus. However, the immunological mechanisms underlying these changes have been less explored. Research has demonstrated alterations in cytokines following physical activity, but the changes in these cytokines and the balance achieved among them in response to different types of exercise require more detailed investigation.

What this study adds?

The present study confirms changes in the balance of TGF-β and IL-17 cytokines, particularly during the third trimester of pregnancy. Nevertheless, future studies should consider examining the responses of the cells producing these cytokines.

Organ Cross-Talk Tips:

- Exercise-induced changes in maternal TGF-β/IL-17 ratios correlate with improved neonatal outcomes, suggesting exercise optimizes tissue cross-talk mechanisms.

Acknowledgements

The authors sincerely thank all the participants in this study.

Funding

This work was supported by the Research Center of Tarbiat Modares University (TMU).

Compliance with ethical standards

Conflict of interest The authors of this research article have no financial and personal conflict of interest statement.

Ethical approval Ethical approval for the study involving pregnant participants was obtained from the Research Ethics Committee in Biomedical Studies at Tarbiat Modares University, Iran (Approval ID: IR.MODARES.REC.1399.122). All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the specific ethical guidelines for research involving pregnant individuals.

Written informed consent was obtained from all participants after providing detailed information about the study's objectives, procedures, and potential risks or benefits. Participants were informed of their right to withdraw at any stage without any consequences. The exercise intervention was designed to ensure the safety of both the pregnant participants and their fetuses, following established guidelines for physical activity during pregnancy. The study was closely monitored by medical professionals to minimize any risks.

Informed consent performed

Author contributions

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

References

Acosta-Manzano, P., Coll-Risco, I., Van Poppel, M. N. M., Segura-Jiménez, V., Femia, P., Romero-Gallardo, L., . . . Aparicio, V. A. (2019). Influence of a Concurrent Exercise Training Intervention during Pregnancy on Maternal and Arterial and Venous Cord Serum Cytokines: The GESTAFIT Project. J Clin Med, 8(11). doi: https://doi.org/10.3390/jcm8111862

Amani Shalamzari, S., Agha Alinejad, H., Gharakhanlou, R., Molanouri Shamsi, M., & Talebi Badrabadi, K. (2009). The effect of body composition and physical activity on basal levels of insulin, glucose, IL-18, IL-6 & CRP and their relationship with insulin resistance. Iranian journal of endocrinology and metabolism, 11(6), 699-706.

Apgar, V. (1953). A proposal for a new method of evaluation of the newborn infant. Curr Res Anesth Analg, 32(4), 260-267.

Artal, R., & O'Toole, M. (2003). Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period. Br J Sports Med, 37(1), 6-12; discussion 12. doi: https://doi.org/10.1136/bjsm.37.1.6

Baffour-Awuah, B., Pearson, M. J., Dieberg, G., Wiles, J. D., & Smart, N. A. (2023). An evidence-based guide to the efficacy and safety of isometric resistance training in hypertension and clinical implications. Clinical Hypertension, 29(1), 9. doi: https://doi.org/10.1186/s40885-022-00232-3

Bernhardt, G. V., Shivappa, P., Bernhardt, K., Bhat, S., Pinto, J. R. T., Jhancy, M., & Kumar, S. (2022). Markers of inflammation in obese pregnant women: Adenosine deaminase and high sensitive C – reactive protein. European Journal of Obstetrics & Gynecology and Reproductive Biology: X, 16, 100167. doi: https://doi.org/10.1016/j.eurox.2022.100167

Bodnar, L. M., Ness, R. B., Harger, G. F., & Roberts, J. M. (2005). Inflammation and Triglycerides Partially Mediate the Effect of Prepregnancy Body Mass Index on the Risk of Preeclampsia. American Journal of Epidemiology, 162(12), 1198-1206. doi: https://doi.org/10.1093/aje/kwi334

Calder, P. C. (2010). Omega-3 fatty acids and inflammatory processes. Nutrients, 2(3), 355-374. doi: https://doi.org/10.3390/nu2030355

Catalano, P. M., & Shankar, K. (2017). Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. Bmj, 356, j1. doi: https://doi.org/10.1136/bmj.j1

Chaabene, H., Prieske, O., Herz, M., Moran, J., Höhne, J., Kliegl, R., . . . Granacher, U. (2021). Home-based exercise programmes improve physical fitness of healthy older adults: A PRISMA-compliant systematic review and meta-analysis with relevance for COVID-19. Ageing Research Reviews, 67, 101265. doi: https://doi.org/10.1016/j.arr.2021.101265

Cilar Budler, L., & Budler, M. (2022). Physical activity during pregnancy: a systematic review for the assessment of current evidence with future recommendations. BMC Sports Science, Medicine and Rehabilitation, 14(1), 133. doi: https://doi.org/10.1186/s13102-022-00524-z

Cirulli, F., De Simone, R., Musillo, C., Ajmone-Cat, M. A., & Berry, A. (2022). Inflammatory Signatures of Maternal Obesity as Risk Factors for Neurodevelopmental Disorders: Role of Maternal Microbiota and Nutritional Intervention Strategies. Nutrients, 14(15). doi: https://doi.org/10.3390/nu14153150

Dennis, A. T., Salman, M., Paxton, E., Flint, M., Leeton, L., Roodt, F., . . . Dyer, R. A. (2019). Resting Hemodynamics and Response to Exercise Using the 6-Minute Walk Test in Late Pregnancy: An International Prospective Multicentre Study. Anesth Analg, 129(2), 450-457. doi: https://doi.org/10.1213/ane.0000000000003818

Djurovic, S., Schjetlein, R., Wisløff, F., Haugen, G., Husby, H., & Berg, K. (1997). Plasma concentrations of Lp(a) lipoprotein and TGF-beta1 are altered in preeclampsia. Clin Genet, 52(5), 371-376. doi: https://doi.org/10.1111/j.1399-0004.1997.tb04356.x

Gascoigne, E. L., Webster, C. M., Honart, A. W., Wang, P., Smith-Ryan, A., & Manuck, T. A. (2023). Physical activity and pregnancy outcomes: an expert review. Am J Obstet Gynecol MFM, 5(1), 100758. doi: https://doi.org/10.1016/j.ajogmf.2022.100758

Gleeson, M., Bishop, N. C., Stensel, D. J., Lindley, M. R., Mastana, S. S., & Nimmo, M. A. (2011). The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol, 11(9), 607-615. doi: https://doi.org/10.1038/nri3041

González-Gil, E. M., Santaliestra-Pasías, A. M., Buck, C., Gracia-Marco, L., Lauria, F., Pala, V., . . . Moreno, L. A. (2022). Improving cardiorespiratory fitness protects against inflammation in children: the IDEFICS study. Pediatric Research, 91(3), 681-689. doi: https://doi.org/10.1038/s41390-021-01471-0

Guinhouya, B. C., Duclos, M., Enea, C., & Storme, L. (2022). Beneficial Effects of Maternal Physical Activity during Pregnancy on Fetal, Newborn, and Child Health: Guidelines for Interventions during the Perinatal Period from the French National College of Midwives. J Midwifery Womens Health, 67 Suppl 1(Suppl 1), S149-s157. doi: https://doi.org/10.1111/jmwh.13424

Hauguel-de Mouzon, S., & Guerre-Millo, M. (2006). The placenta cytokine network and inflammatory signals. Placenta, 27(8), 794-798. doi: https://doi.org/10.1016/j.placenta.2005.08.009

Hekmatikar, A. H. A., Shamsi, M. M., Ashkazari, Z. S. Z., & Suzuki, K. (2021). Exercise in an Overweight Patient with Covid-19: A Case Study. Int J Environ Res Public Health, 18(11). doi: https://doi.org/10.3390/ijerph18115882

Kubler, J. M., Clifton, V. L., Moholdt, T., & Beetham, K. S. (2022). The effects of exercise during pregnancy on placental composition: A systematic review and meta-analysis. Placenta, 117, 39-46. doi:10.1016/j.placenta.2021.10.008

Lawrence, S. M., Ruoss, J. L., & Wynn, J. L. (2018). IL-17 in neonatal health and disease. Am J Reprod Immunol, 79(5), e12800. doi: https://doi.org/10.1111/aji.12800

Li, Y., Chen, J., Lin, Y., Xu, L., Sang, Y., Li, D., & Du, M. (2021). Obesity Challenge Drives Distinct Maternal Immune Response Changes in Normal Pregnant and Abortion-Prone Mouse Models. Front Immunol, 12, 694077. doi: https://doi.org/10.3389/fimmu.2021.694077

Mahdieh, M. S., Maryam, J., Bita, B., Neda, F., Motahare, M., Mahboobeh, B., . . . Kalani Behrooz, S. (2023). A pilot study on the relationship between Lactobacillus, Bifidibactrium counts and inflamm-atory factors following exercise training. Arch Physiol Biochem, 129(3), 778-787. doi: https://doi.org/10.1080/13813455.2021.1871763

Mokhtarzade, M., Molanouri Shamsi, M., Abolhasani, M., Bakhshi, B., Sahraian, M. A., Quinn, L. S., & Negaresh, R. (2021). Home-based exercise training influences gut bacterial levels in multiple sclerosis. Complementary Therapies in Clinical Practice, 45, 101463. doi: https://doi.org/10.1016/j.ctcp.2021.101463

Mor, G., Cardenas, I., Abrahams, V., & Guller, S. (2011). Inflammation and pregnancy: the role of the immune system at the implantation site. Ann N Y Acad Sci, 1221(1), 80-87. doi: https://doi.org/10.1111/j.17496632.2010.05938.x

Moroishi, Y., Salas, L. A., Zhou, J., Baker, E. R., Hoen, A. G., Everson, T. M., . . . Karagas, M. R. (2023). Umbilical cord blood immune cell profiles in relation to the infant gut microbiome. iScience, 26(1). doi: https://doi.org/10.1016/j.isci.2022.105833

Muy-Rivera, M., Sanchez, S. E., Vadachkoria, S., Qiu, C., Bazul, V., & Williams, M. A. (2004). Transforming growth factor-beta1 (TGF-beta1) in plasma is associated with preeclampsia risk in Peruvian women with systemic inflammation. Am J Hypertens, 17(4), 334-338. doi: https://doi.org/10.1016/j.amjhyper.2003.12.010

Osborne, L. M., Brar, A., & Klein, S. L. (2019). The role of Th17 cells in the pathophysiology of pregnancy and perinatal mood and anxiety disorders. Brain Behav Immun, 76, 7-16. doi: https://doi.org/10.1016/j.bbi.2018.11.015

Physical Activity and Exercise During Pregnancy and the Postpartum Period: ACOG Committee Opinion, Number 804. (2020). Obstet Gynecol, 135(4), e178-e188. doi: https://doi.org/10.1097/aog.0000000000003772

Pieren, D. K. J., Boer, M. C., & de Wit, J. (2022). The adaptive immune system in early life: The shift makes it count. Front Immunol, 13. doi: https://doi.org/10.3389/fimmu.2022.1031924

Ross, R., Dagnone, D., Jones, P. J., Smith, H., Paddags, A., Hudson, R., & Janssen, I. (2000). Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial. Ann Intern Med, 133(2), 92-103. doi: https://doi.org/10.7326/0003-4819-133-2-200007180-00008

Saito, S., Tsuda, S., & Nakashima, A. (2023). T cell immunity and the etiology and pathogenesis of preeclampsia. Journal of Reproductive Immunology, 159, 104125. doi: https://doi.org/10.1016/j.jri.2023.104125

Sanjabi, S., Oh, S. A., & Li, M. O. (2017). Regulation of the Immune Response by TGF-β: From Conception to Autoimmunity and Infection. Cold Spring Harb Perspect Biol, 9(6). doi: https://doi.org/10.1101/cshperspect.a022236

Santos, S., Voerman, E., Amiano, P., Barros, H., Beilin, L. J., Bergström, A., . . . Jaddoe, V. (2019). Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. Bjog, 126(8), 984-995. doi: https://doi.org/10.1111/1471-0528.15661

Shin, D., & Song, W. O. (2015). Prepregnancy body mass index is an independent risk factor for gestational hypertension, gestational diabetes, preterm labor, and small- and large-for-gestational-age infants. The Journal of Maternal-Fetal & Neonatal Medicine, 28(14), 1679-1686. doi: https://doi.org/10.3109/14767058.2014.964675

Spence, T., Allsopp, P. J., Yeates, A. J., Mulhern, M. S., Strain, J. J., & McSorley, E. M. (2021). Maternal Serum Cytokine Concentrations in Healthy Pregnancy and Preeclampsia. J Pregnancy, 2021, 6649608. doi: https://doi.org/10.1155/2021/6649608

Tang, C., & Hu, W. (2023). The role of Th17 and Treg cells in normal pregnancy and unexplained recurrent spontaneous abortion (URSA): New insights into immune mechanisms. Placenta, 142, 18-26. doi: https://doi.org/10.1016/j.placenta.2023.08.065

Topper, J. N. (2000). TGF-beta in the cardiovascular system: molecular mechanisms of a context-specific growth factor. Trends Cardiovasc Med, 10(3), 132-137. doi: https://doi.org/10.1016/s1050-1738(00)00061-x

Witvrouwen, I., Mannaerts, D., Van Berendoncks, A. M., Jacquemyn, Y., & Van Craenenbroeck, E. M. (2020). The Effect of Exercise Training During Pregnancy to Improve Maternal Vascular Health: Focus on Gestational Hypertensive Disorders. Front Physiol, 11, 450. doi: https://doi.org/10.3389/fphys.2020.00450

Zhang, J.-W., Guan, J.-Q., & Zhong, Y.-X. (2023). Association of prenatal obesity and cord blood cytokine levels with allergic diseases in children: A 10-year follow-up cohort study. Heliyon, 9(6), e17375. doi: https://doi.org/10.1016/j.heliyon.2023.e17375