Influence of Gestational Exercise on One-Month Infant Resting Autonomic and Cardiac Control

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**Abstract**

**Objective:** The purpose of this study is to determine the effects of exercise type during pregnancy on an infant's cardiac and autonomic nervous systems at one month of age. This research is essential because of the increasing development of cardiovascular disease in adults and children. Learning what type of gestational exercise influences the cardiac and autonomic nervous system could program the next generation for a healthier life before birth. If an infant is born with these changes, then the likelihood of developing cardiovascular disease, and its risk factors, might be decreased. I hypothesize that the groups exercising at moderate intensity (aerobic, combination, and resistance) will have improved infant heart outcomes compared to the control group (stretching/breathing).

**Method:** Data was collected from 74 pregnant women who completed the research study. These women also returned with their infant for a follow-up visit at one month of age. Throughout the period of study, women completed 50-minute sessions three times per week from 16 weeks to the time of delivery. Women were trained in aerobic, resistance, combination (aerobic+resistance), or stretching/breathing (control) exercises. At the one-month infant visits, cardiac and autonomic nervous system data (i.e., heart rate= HR, heart rate variability= HRV, and breathing rate) were measured via Hexoskin Smart Garment technology. All tests performed were set to an alpha level

of .05 and a power of 95%. All analysis tests were done using IBM SPSS Statistics Version 28. For regression analysis, exercise groups were given numbers based on increasing intensity.

**Results:** When comparing maternal and infant descriptors between groups, maternal prepregnancy BMI (body mass index) was different between groups (p=.03). There were no other differences in maternal and infant descriptors between groups. Post-hoc Tukey analysis indicates these differences are between Resistance to Combination (p=0.01), as well as Resistance to Control (p=0.01). Regression analysis indicates exercise group, numbered by intensity, predicts one-month-old infant HR (p=.03). Similarly, gestational age is a predictor of one-month-old infant RMSSD (p=.03). Although not significant, the trends of large effect sizes demonstrate that male infants have increased HRV and lower resting HR indicative of more mature autonomics relative to their female counterparts.

**Discussion:** Based on infant outcomes, the data demonstrates all exercise modes are safe to perform while pregnant. It also shows a relationship between exercise intensity and one-month infant resting heart rate. Male infants also have more mature cardiac autonomic nervous system measures. Further research is necessary to determine if these patterns persist with a larger sample and as the infants develop. This research will allow a better understanding of how moderate intensity exercise during pregnancy affects infant cardiac and autonomic nervous system. That knowledge, if applied, could decrease the chance of offspring developing CVD and its risk factors before birth, thus, ultimately decrease the deaths caused by CVD in the next generation.

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List of Abbreviations

| | |
|---|---|
| CVD | Cardiovascular Disease |
| ANS | Autonomic Nervous System |
| ACOG | The American College of Obstetricians |
| HR | Heart Rate |
| HRV | Heart Rate Variability |
| BR | Breathing Rate |
| BPM | Beats Per Minute |
| BrPM | Breathing Rate Per Minute |
| RMSSD | Root Mean Square of Successive Differences |
| ms | Milliseconds |
| MCG | Magnetocardiogram |
| GA | Gestational Age |
| FHR | Fetal Heart Rate |
| ACSM | American College of Sports Medicine |
| GDM | Gestational Diabetes Mellitus |
| BP | Blood Pressure |
| RPE | Rate of Perceived Exertion |
| THR | Target Heart Rate |
| AT | Athletic Training/Exercise |
| RT | Resistance Training/Exercise |
| CT | Combination Training/Exercise |
| CON | Control |
| BMI | Body Mass Index |
| ECG | Electrocardiography |
| ANOVA | Analysis of Variance |
| METS | Metabolic Equivalents |

# Chapter 1: Introduction

Today, the leading cause of death in humans is heart disease, also known as cardiovascular disease (CVD). CVD includes a group of diseases that affect the heart and blood vessels. These diseases include but are not limited to arrhythmia, coronary artery disease, heart failure, and valve disease. The development of CVD varies by the specific type of disease. However, major reasons for the development of CVD include plaque buildup in the arteries, heart muscle scarring, genetics, and aging (Cleveland Clinic, 2022). Risk factors that increase the likelihood of developing conditions that lead to CVD include obesity, Type II diabetes, a sedentary lifestyle, and having a family history of heart disease or CVD (Felman, 2021).

For pregnant women in particular, studies have started to support the idea that there are positive maternal outcomes with moderate-intensity gestational exercise. These positive maternal outcomes also suggest a positive influence on the fetal Autonomic nervous system (ANS) and fetal heart development (Cooper et al., 1987; May et al., 2010). Further research on gestational exercise and its effects on an infant's heart development could help prove that the earliest time to improve cardiovascular autonomic health is before birth.

Moderately intense exercise during pregnancy is considered to be overall safe, if not beneficial, for both mother and offspring. With that information given, an alarmingly high percentage of women still do not meet the American College of Obstetricians and Gynecologists (ACOG) guidelines for exercise while pregnant. In the past decade, researchers have become increasingly more interested in gestational exercise and how it affects the fetus, and the infant once it is born. With this information continuing to be provided through peer-reviewed publications, the hope would be that more women feel comfortable and safe trying to meet the exercise guidelines. For example, in 2017, the latest edition of the ACOG guidelines was published. These guidelines include accumulating 150 minutes of moderate-intensity exercise each week and exercising a minimum of three days per week– although it is recommended that pregnant women exercise daily– incorporating aerobic and resistance exercises and cool-downs and warm-ups (U.S. Department of Health and Human Services, 2018). In 2019, yoga and gentle stretching were added to the guidelines based on Canadian recommendations (Mottola et al., 2018a). Additionally, each physical activity program should be individualized based on the situation, experience, and current health status of the expectant mother (Bauer, 2020). With gestational exercise, following the ACOG guidelines (2018), potential benefits include the fetal cardiac autonomic system being more mature. These benefits are hoped to persist in the infant throughout childhood. With these persisting benefits, preventing CVD risk factors from occurring early in life will decrease the potential development of heart disease.

Determination of fetal heart and autonomic nervous system development includes measuring heart rate (HR), heart rate variability (HRV), and breathing rate (BR). HR and HRV measure the heart's development, while BR measures the development of the respiratory system. These systems are intimately linked by hemodynamic, mechanical, and neurohumoral pathways (Cross et al., 2020). Both the cardiac and the respiratory systems are controlled by the autonomic nervous system (ANS). The ANS works behind the scenes, automatically regulating heart rate, blood pressure, and breathing. The ANS is divided into two components: the sympathetic and parasympathetic nervous systems. These systems are also known as the fight or flight mechanism and the relax response, respectively (McCorry, 2007). Thus, measuring HR, HRV, and BR provides a good indicator of the maturation of cardiac and autonomic nervous system development.

Recent epidemiologic studies have confirmed that high resting HR and low HRV values are independent predictors of cardiovascular mortality and sudden cardiac death (Fox et al., 2007; Goldenberg et al., 2019). The normal range for HR in infants 0-3 months of age is 123-164 beats per minute (BPM). A normal range for BR in infants 0-3 months is reported to be 34-57 breaths per minute (BrPM) (Fleming et al., 2011). Due to a lack of research in this area, specific ranges for normal infant HRV are still not determined. However, a study completed by Patural et al., (2019) followed infants from birth to 2 years of age and recorded measures of the root mean square of successive differences between normal heartbeats (RMSSD). RMSSD is a timedependent measure of HRV that is associated with short-term, rapid changes in heart rate. RMSSD is the primary time-domain measure used to estimate the vagally mediated changes reflected in HRV (Stein et al., 1994). The Patural (2019) study recorded RMSSD measures at 0, 6, 12, 18, and 24 months of age.  Additionally, it reported that normal ranges for RMSSD in newborn infants are between 16.6-47.5 milliseconds(ms). Infants at six months were reported to have a normal range of 15.9-48.2(ms). When comparing these ranges, the differences are negligible. The lack of differences in these ranges suggests that no significant changes in RMSSD are seen in the age range of infants from newborn to 6 months.

With HR, HRV, and BR being known factors to measure the development of the cardiac autonomic nervous system, the present study focused on comparing these measures in 4 gestational exercise groups in infants at one month of age 1. The exercise groups were labeled Resistance, Aerobic, and Combination– to clearly describe the type of exercise–  with the control group labeled Breathing/Stretching. Between these groups, we aim to determine which type of exercise best affects the infant's cardiac and autonomic outcomes. This study hypothesizes that all moderate-intensity exercise groups will show a decrease in HR and BR, and an increase in

RMSSD. This effort is critical because it can support the idea that gestational exercise benefits the infant's cardiac autonomic nervous systems development. With effects like this, the possibility of decreasing the risk of developing chronic diseases such as CVD exist before birth. Given that CVD is the number one killer in the United States–this information is essential to improve public health implications.

## Chapter 2: Literature Review

Scientific studies that have met the guidelines of the ACOG have shown numerous benefits for pregnant women. Some benefits of exercising while pregnant include decreasing the risk of gestational diabetes, preeclampsia, cesarean delivery, appropriate gestational weight gain, improvement in general fitness, and strengthening of heart and blood vessels (Obstetrics & Gynecology, 2020).

Although more is known about the effects of exercise on pregnant women, there is limited knowledge on the other individual involved, the developing infant. Studies focusing on fetal development and outcomes from gestational exercise are critical. Specifically, we can learn how to help establish a healthy lifestyle before birth. Although the research on gestational exercise on infants is still limited, there are findings that support the idea of health benefits for the fetus after birth.

Since heart disease is the leading cause of death in the United States (Centers for Disease Control and Prevention., 2022), it is also essential to focus on the heart function of the offspring. Based on the limited studies published, researchers have found a link between the fetal cardiovascular system and maternal physical activity (May et al., 2014a, p. 367). Some studies report that with regular maternal physical activity throughout pregnancy, fetal HR is decreased, and HRV is increased (May et al., 2010, p. 215). HRV is a measure of the variation in the time between heartbeats. This variation is controlled by a part of the nervous system called the autonomic nervous system (ANS). As previously stated, the ANS works regardless of our desire, and regulates HR, blood pressure, breathing, and digestion. HRV has become a non-invasive way to identify ANS imbalances. In recent years a relationship has been found between a low

HRV and an increased risk of death and cardiovascular disease (Goldenberg et al., 2019). The measures of HR and HRV have been used during pregnancy to determine the overall health and appropriate nervous system development of the fetus (May et al., 2014b, p. 367). There is evidence to support a dose-response relationship between maternal physical activity levels and fetal cardiac autonomic nervous system control.

In one study by May et al., (2014b), HRV was compared in women who exercised a minimum of 30 minutes, three or more days a week, with women who exercised less (the control group). Measurements were taken at three different points during pregnancy (28, 32, and 36 weeks of gestation). At gestational week 36, HRV was significantly higher in women who exercised compared to the control group. In another study done by May, Scholtz et al. (2014a), comparison of HRV in infants was made based on two groups: women who exercised while pregnant for 30 minutes three times a week, and a control group who exercised less. Infants in the group whose mothers exercised had a higher RMSSD. This suggests that gestational exercise benefits the infant's cardiac function with a lower HR and increased HRV. What we do not know is which type of exercise is most beneficial to the cardiac function of the infant. Therefore, this literature review focuses on how different types of maternal exercise affects the offspring’s cardiac and autonomic nervous system functions.

**Aerobic Effects on Fetus**

To date, a limited number of studies have explicitly focused on the effects of intrauterine exercise on the fetus and infant. Of the studies published, aerobic exercise is the most common when looking at these effects. One study in particular (May et al., 2010, p. 215), compares exercising to non-exercising pregnant women. Women were assigned to the exercise group if they continued moderate to vigorous aerobic exercise throughout their pregnancy for a minimum of 30 minutes, three times a week. Women in the non-exercising (control) group reported not participating in moderate or vigorous aerobic exercise while pregnant. In total, 61 pregnant women were involved in this study: 26 in the exercise group and 35 in the control group. All participants were asked to have a magnetocardiogram (MCG) at 28, 32, and 36 weeks gestational age. An MCG is a non-invasive technology able to measure the fetal QRS complex. It measures magnetic fields produced by electrical currents in the heart.

The results of this study reveal a significantly lower fetal HR (p=.023) and an increased HRV (p=.024) in the exercise group after adjusting for gestational age and fetal activity state. Additionally, HRV in both time and frequency domains increases with gestational age, which is also seen in similar reports (see for example, David et al., 2007). May et al., (2010, p. 215) concluded that maternal exercise throughout gestation results in a significantly lower fetal HR and increased fetal HRV. This suggests that regular maternal aerobic exercise during a healthy/low-risk pregnancy positively influences the development of fetal cardiac autonomic control.

Another study examined the impact of maternal exercise on fetal breathing and movement; measures used to assess fetal well-being. Winn et al. (1994) had 12 pregnant women between the gestation age of 26-36 weeks exercise on a treadmill using the Bruce protocol. Participants exercised on the treadmill until they reached their 75% age-predicted heart rate maximum. The test monitored fetal breathing and body movement 20 minutes before and after the exercise protocol. This study found a significant decrease in the total duration and frequency of fetal breathing and body movements following acute maternal exercise.

**Aerobic Effects on Infant**

Aerobic exercise is generally utilized in studies investigating gestation exercise effects. However, minimal studies have been done looking at these effects on the infant after it is born. Therefore, conducting more studies that do look after birth is vital to see if the fetus's benefits persist.

In a study completed by May et al. (2010), the study population consisted of a subset of infants born to women enrolled in a longitudinal study comparing maternal aerobic exercise on fetal ANS. A second study focused on maternal aerobic exercise and infant cardiac ANS (May et al., 2014a). Of the 67 women from the initial study, 46 agreed to participate in this follow-up study and 43 of those women were included in the data. When the infant reached 1-month, HRV was analyzed in both time and frequency domains. The goal of this study was to show that moderate to vigorous maternal physical activity of 30 minutes a day, at least three days a week, during pregnancy significantly increases an infant's HRV and decreases fetal HR. Results of this study show that the infant's outcomes closely correspond with the fetal HR and HRV predictions.

Results of the study showed that infants born to women who engaged in moderate to vigorous aerobic exercise had significantly higher short-term HRV (RMSSD; $p=.01$) at one month of age than those born to women in the control group. Also, infant HR was lower (147 vs. 153 beats per minute) in the exercise group compared to the control but did not reach significance ($p=.018$). During this study, researchers aimed to maintain a constant awake and alert state in the infant.  When comparing HR patterns of the infant with the-fetus,  an observation of greater excursions in HR patterns (greater accelerations with longer durations) was seen in the one-month infant. This observation was reported to possibly contribute to the sample variability in the follow-up infant study. It was assumed that the sample variability reduced the potential to detect meaningful differences in the one-month infants.

In conclusion, this study found that the programming effects on the infant via regular maternal physical activity during pregnancy may be the earliest intervention to improve cardiac autonomic function. It also concludes that infants born to women who had participated in regular physical activity during pregnancy continued to have higher HRV during infancy. This suggests that a developing cardiac autonomic nervous system is sensitive to the effects of maternal physical activity and is a potential target for fetal programming (May et al., 2014b, p. 35).

**Resistance Effects on Fetus**

In recent years, studies have shown that gestational resistance exercise poses no harm to pregnant women and potentially provides health benefits. Since this information was published, more women have partaken in gestational resistance training. As of yet, although the popularity of gestational resistance training has increased, few studies have reported on the fetal outcomes resulting from maternal resistance exercise.

One of the few studies mentioned above was conducted by Bgeginski et al. (2015). This study took ten pregnant women between 22-24 weeks gestational age (GA) and had them perform different resistance exercises. These women came in five times at the GA of 22-24, 2832, and 34-36 weeks. The first session was used to familiarize the women with the equipment and to determine the estimated maximum repetition. Resistance exercises were performed at 50% of the estimated repetition max for the following four sessions. Fetal heart rate (FHR) was assessed during this with a cardiotocograph. No significant differences in FHR between exercises at 22-24 weeks (p=.34), 28-30 weeks (p=.75), and 34-36 (p=.38) were seen in the analysis.

In a second study by Beilock et al. (2001), 12 healthy pregnant women in their third trimester and 12 healthy non-pregnant women were utilized. It was found that the frequency, intensity, and time of the resistance training are inversely related to fetal complications. For example, increased resistance training is associated with a decreased likelihood of fetal complications during pregnancy (p. 40). While in yet another study, it was found that there were associations between type of maternal activity and fetal HRV. The time spent doing continuous activity was associated with evidence of increased parasympathetic control. Additionally, the time engaged in non-continuous activities, like weightlifting, is associated with overall fetal HRV (May et al., 2014b, p. 368). Taken together, these studies suggest that the development of the fetal cardiovascular system responds in different ways to different modes of maternal exercise.

**Resistance Effects on Infant**

In a Medline meta-analysis by Perales et al. (2016), three randomized controlled trials dealt with resistance training and infants. One study done by Barakat et al. (2009) randomly assigned 160 previously sedentary women to either a training (n=80) or a control group (n=80). The exercise group participated in 3 sessions a week for 26 weeks. Training intensity was prescribed to be light to moderate and less than 80% of age predicted HRmax. This included 1 set of 10-12 reps with the use of 3kg barbells or the use of low-to-medium resistance bands. In comparison, the control group was asked to maintain their current activity level. This study found no effects on the newborn outcomes between study groups.

The second study in the Medline meta-analysis by Perales was done by Garshasbi & Faghih Zadeh (2005). This study was a randomized control trial that examined the effect of exercise during pregnancy on low back pain intensity. This study aimed to examine the efficacy of a strengthening exercise program on different muscle groups. This study too, found no differences in the newborn results.

The third study discussed by Perales was conducted by Petrov Fieril et al. (2014). In this study, the exercise group performed high-repetition resistance training using light barbells (1-10 lbs.). The exercise group trained twice weekly for 12 weeks (pregnancy weeks 14-25). This study found significant differences between the control and exercise groups in the newborn's birth weight. The infants delivered by women who participated in the exercise group were significantly heavier than those born to the control group.

Resistance training done by pregnant women has not been studied in great depth. Only in recent years have the health benefits of gestational resistance exercise become increasingly recognized and considered safe.  For many years, it was thought to be unsafe to do resistance training while pregnant (Barakat & Perales, 2016). That being said, a limited number of studies about gestational resistance exercise focus solely on the cardiac and autonomic nervous systems of the infant. More information is needed about how gestational resistance training affects the infant's heart function and development. With that additional information, the question of what type of gestational exercise most benefits the infant's cardiac function (HR and HRV) would be more easily addressed.

### Combination Effects on Fetus

Knowledge about the effects of maternal combination training on infant outcomes is still limited. Although there is some evidence that maternal combination training is associated with an increase in total HRV power– which is similar to aerobic and resistance exercise separately (Price et al., 2012)-- other studies have suggested that the effect of maternal physical activity in women who engage in higher intensity physical activity, is that fetuses develop a lower HR and a higher HRV. This suggests that the intensity and duration of physical activity during pregnancy influence the change observed in fetal cardiac autonomic control (May et al., 2012).

### Combination Effects on Infant

There are few studies focusing on the effects of maternal combination training on the fetus, and there are even fewer studies relating maternal combination training on the infant. Although, in both resistance and aerobic training, as discussed in the above sections, studies reported infants having decreased HR and BR with an increased HRV. The same results would be expected to be found in combination training since this involves both aerobic and resistance training. The previous studies of both aerobic and resistance training found decreased HR and BR and increased HRV, so combination training (including both of these types of exercise) will likely lead to similar results. Nonetheless, more studies incorporating gestational combination training need to be completed in order to determine the effects on the infant's development and the function of the infant's heart.

**Light Intensity Activity on Fetus**

Stretching and breathing techniques, such as yoga, has been practiced for countless years, but recently there has been a focus on the benefits of yoga during pregnancy. The American College of Sports Medicine (ACSM) guidelines suggest that physical activity, including yoga, should be incorporated during pregnancy (Bauer, 2020). This form of physical activity is recommended due to the different choices one has, such as which postures to use and how to modify them as gestational age progresses (Uebelacker et al., 2015). Even with the popularity of yoga, there is limited research focusing on yoga during pregnancy and its effects on the fetus and infant.

One of the few studies focusing on prenatal yoga and its effects on the fetus was conducted by Gavin et al., (2018) focused on maternal and fetal responses to moderate-intensity yoga in pregnant women during their third trimester. Exercise in this study consisted of four phases: 20- minute rest, 50-minute standard prenatal yoga, 10-minute meditation, and 20-minute recovery. Throughout the yoga session, fetal and maternal HR was continuously recorded for the 19 participants. While maternal HR increased during exercise, the fetal HR was reported to have fluctuated only slightly throughout the yoga session and there were no significant fetal HR decelerations.

Although this study gives information about how the fetal heart responds to prenatal yoga, it does not provide enough information about how beneficial it is for the fetus's heart function and development. The field would benefit from understanding how prenatal yoga affects fetal heart development.

**Light intensity activity on Infant**

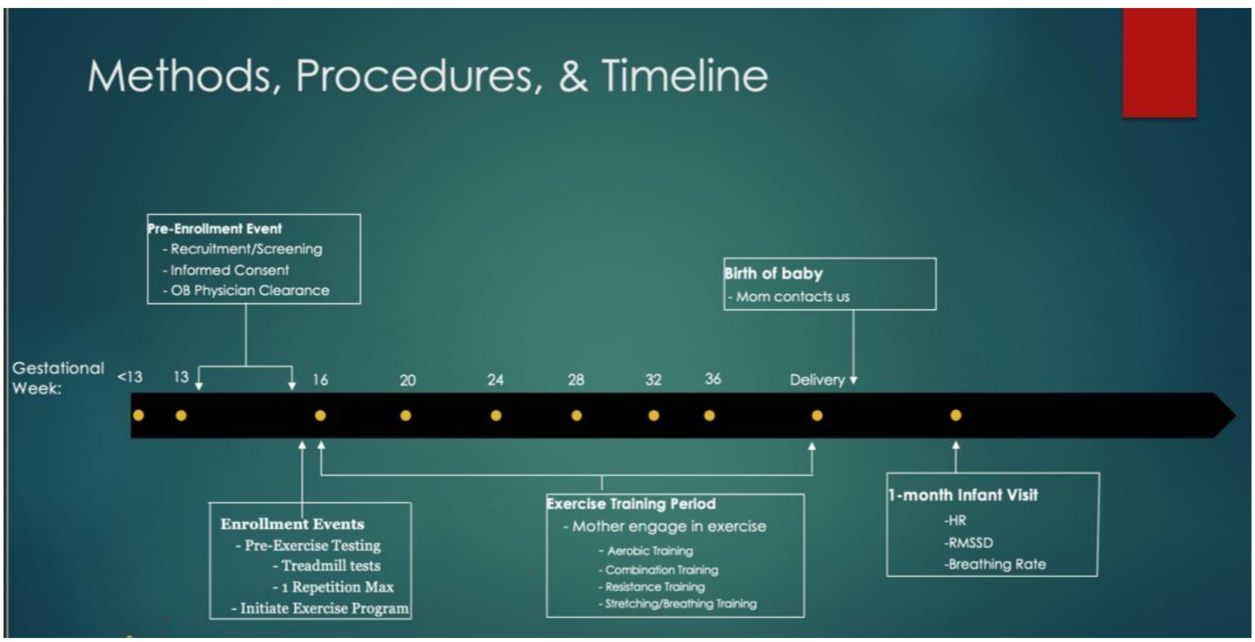
The question of how prenatal yoga affects an infant is also unanswered to date. In most studies, gestational yoga exercise is typically used as a control group compared to other aerobic and resistance exercises. Yoga might be a lower-intensity exercise, but it still increases HR for both mother and fetus. More studies are needed to confirm how much gestational yoga can affect the development and function of the infant's heart. However, with the recent increase in the encouragement of gestational exercise, ideally this information will be understood sooner rather than later.

In summary, gestational exercise throughout pregnancy has proven safe and beneficial for mother and child. Research has shown that there are effects on the developing fetus' autonomic nervous system with gestational exercise. More research needs to be completed to determine which exercise mode during pregnancy presents long-term benefits in infant health.

## Chapter 3: Methods

This randomized control trial aimed to determine what type of gestational exercise influences cardiac and autonomic function in 1-month infants. The 1-month infant heart function was measured by HR and RMSSD, while autonomic control was determined by RMSSD and BR measures. I hypothesized that in utero, exposure to moderate-intensity exercise would show improved measures of infant heart and autonomic function at one month, compared to one- month infants in the control group. An overview of the study design includes the following variables: Preenrollment visits, Enrollment Visits, Exercise Training Period, Birth of Baby, and 1-Month infant Visits (Figure 1).

Figure 1. Methods, Procedures, And Timeline




**Participants:**

All participants were enrolled in the pregnancy study conducted at East Carolina University. This study focused on moderate-intensity supervised exercise during pregnancy on fetal and infant health outcomes. Participants were recruited by flyers distributed at local obstetric offices and local businesses, by word of mouth, and on social media. Eligibility criteria to participate included: women being between the ages of 18-40 years old, in the first trimester (16 weeks gestation or less) of pregnancy, less than 300 pounds, and willing to participate in weekly exercise. All potential participants were screened to determine eligibility of participation in the study. Women were excluded for the following reasons: 1) current use of alcohol, tobacco, or recreational drugs; 2) current use of medications that affect fetal growth; 3) pre-pregnancy conditions including diabetes, hypertension, cardiovascular disease, or any comorbidities known to affect fetal growth or well-being; 4) lack of transportation or inability to speak English. Any participant diagnosed with gestational diabetes mellitus (GDM) was allowed to continue participating in the study. Once eligibility was determined, an informational visit occurred, during which women were informed of all study procedures. They signed a consent form for themselves and their child if they chose to participate.

**Pre-exercise Testing**

After consent, the participant was scheduled for pre-exercise testing. There were two exercise testing protocols: 1) submaximal exercise test to determine individual aerobic capacity and 2) one-repetition maximum testing to determine individual muscular strength. Before exercise testing started, the participant’s resting heart rate and blood pressure were measured. These measurements determined baseline resting values. The participant's heart rate was determined by wearing a Polar FS2C HR wristwatch and chest band. Resting blood pressure was measured using a sphygmomanometer with a cuff and stethoscope.

The Balke submaximal treadmill test was used to determine $VO_{2peak}$ and has been previously validated in the pregnant population (Barker et al., 2005). To start, the participant stood on the treadmill for three minutes to determine the baseline oxygen consumption, using an indirect calorimeter. The participant's heart rate was continuously monitored during rest and exercise for all protocol procedures using the Polar FS2C watch and chest band. The Balke submaximal Treadmill test includes three main stages; warm-up, exercise, and cool-down. The warm-up was five minutes, during which the participant walked at a constant speed of 3 mph at a 0% grade. Next, the participant entered the exercise phase. This phase consisted of 10 or more stages, lasting 2 minutes each. In stages 1-7, the speed was held at 3 mph while the grade increased by 2% every two minutes. This change in grade signaled the change in the stage. In stages 7-10, the participant remained at a constant 12% grade, and the speed increased by 2 mph. As stated by the ACSM, the exercise test was immediately terminated if the participant began to experience symptoms such as shortness of breath, wheezing, leg cramps, light-headedness, and either excessive rise or drop in blood pressure (BP). Following this phase, the participant entered the cool-down, which consisted of walking at a slow, low intensity. The speed during this phase ranged from 1.5-2 mph, at a 0% grade. HR was monitored every minute for five minutes, which ideally determined a healthy decline back to baseline vitals. HR was continuously monitored and recorded just before the end of every stage: at minute 2:30 of the resting phase, minute 7:30 of the warm-up, every two minutes during the exercise stages before grade increase, and every minute on the minute of the cool-down phase. BP was measured during the same times as HR: within the last minute of the resting phase, warm-up, and each exercise stage. BP was only measured and recorded during the last minute of the cool-down.

The rate of perceived exertion (RPE) based on the Borg scale (6-20) was recorded at twominute intervals throughout the test. The Borg Scale is a visual, but numerical, representation of subjective physical strain due to exercise. On the scale, 6 is described as the lowest to signify no exertion, and 20 is the highest to signify maximal exertion. Ratings within the range of 6 to 12 are considered light to moderate exertion, with increased breathing rate and muscle engagement. Ratings 13 or 14 are considered moderate exertion. Any rating of 15 or above is considered hard. A rating of 17 or above is considered extremely hard, with increased muscular pain and difficulty breathing. RPE is correlated with exercise HR and work rates and has a sizable interindividual variability regarding interpretation.

Oxygen consumption (VO2, ml O2 · kg-1 · min-1) was assessed using breath-by-breath analysis. The average O2 consumed was recorded in 30-second intervals. $VO_{2peak}$ was determined by identifying the highest amount of oxygen consumed during the test. Subsequently, the participant's target heart rate range (THR) was calculated using HR, corresponding to 40% and 59% of their individual $VO_{2peak}$. This THR represented moderate-intensity exercise and was used to prescribe individual exercise regimens.

Due to COVID during the last year of the study, the submaximal treadmill test could not be administered safely. Therefore, we used published norms for pregnant women to establish a moderate intensity HR range for the participant. See, for example, Mottola et al., (2018b). These published ranges state that pregnant women who wish to exercise at a moderate intensity based on their heart rate reserve should keep their heart rate in the following ranges: 125-146 bpm for women aged 29 and below, and 121-141 bpm for women aged 30 and above.

### 1-Repetition Max Test

Following the submaximal exercise test, participants completed a "one-repetition maximum test" to assess the muscular strength of select major and minor muscle groups. Before executing each resistance exercise, the proper technique was demonstrated to avoid injury and produce accurate estimations of muscular strength. Each exercise required at least three attempts to estimate a one-repetition maximum accurately. Most resistance exercises were performed on Cybex machines which included: leg extension (quadriceps), leg curl (hamstrings), shoulder press (front shoulder, anterior deltoid), chest press (pectoralis major), incline chest press (upper pectoralis major), triceps extension (triceps), latissimus dorsi pull-down (latissimus dorsi), and seated row (trapezius, latissimus dorsi, teres group). Additional exercises were conducted with the use of dumbbells which included: bicep curls (biceps), lateral shoulder raises (deltoid group), and front shoulder raises (anterior deltoid). If a participant could not properly perform an exercise using the Cybex machines or dumbbells, then resistance bands or bodyweight exercises were substituted.

### Randomization

Following the pre-exercise testing, participants were randomized into one of the four groups: aerobic training (AT), resistance training (RT), combination training (CT), or breathing/ stretching (CON). Participants were assigned by a random sequence generator (GraphPad). Due to the nature of an exercise intervention, all participants and trainers were informed of group allocations.

**Exercise Protocol**

All exercise training groups (AT, RT, CT) participated in 50 minutes of moderate intensity (40-59% VO2 peak) exercise three times per week. Each training session began with recording the participant's resting HR and BP. Once these measures were recorded, a 5-minute low-intensity warm-up was completed. After the warm-up, the participant started their 50-minute moderate-intensity workout. A 3-5-minute cool-down then followed this workout. During exercise, maternal HR was continuously monitored by a heart rate monitor (Polar FS2C) to ensure compliance with the intended exercise intensity. A seated HR and resting BP were taken after the completion of each session to ensure participant vitals were at safe resting levels before they went home. It was anticipated that exercise adaptations would occur throughout gestation, most evident being a decrease in maternal HR during exercise sessions. Thus, to ensure that participants maintained progression, the speed, incline, and resistance (appropriate to their assigned group) were increased to ensure that maternal HR remained in the prescribed target heart rate (THR) zone during each session.

After warm-up, the resistance training group performed four resistance exercises, in 2 sets of 12-15 repetitions. The initial workload for each exercise was determined using a resistance of 50-60% of the 1-RM (1 repetition maximum) pre-exercise test following ACSM guidelines (ACSM, 2010, pg. 183-187). The participants executed the same (or similar) resistance exercises as those performed during the 1-RM testing. These exercises were done using Cybex machines and dumbbells, while the core exercises were conducted on a bench or yoga mat. The exercise prescription was adapted for the participant's current week of gestation and comfort level. Progression was determined by the participant's ability to execute the resistance exercise above the prescribed repetition range (12-15). For the large and small muscle groups, the resistance load was increased accordingly with the goal of completing 12-15 repetitions.

The aerobic training group performed their exercise on an aerobic machine based on the participant's individual preference: treadmill, elliptical, seated rower, upright bike, outside walking, and/or recumbent bike. During this exercise session, the participant could perform various forms of aerobic exercise, including alteration of the aerobic machines listed above.

The combination training group incorporated both of the previously described aerobic and resistance exercises. 50% of the session was dedicated to aerobics and 50% to resistance. Following the warm-up, four resistance exercises and ten minutes of aerobic exercise were done to complete one combination. There were five combinations to complete one session. The resistance portion consisted of one set of 12-15 repetitions, as previously described. Before performing exercises, proper form and technique were explained and demonstrated so as to avoid injury and to maximize strength and aerobic capacity improvements.

For women new to exercise, regimens were gently introduced, or even altered, to avoid overtraining or injury. These participants performed exercise at the lowest HR within their target HR zone for the first two weeks of exercising.

The control group completed sessions focused on stretching and proper breathing techniques for 50 minutes, three times per week. Sessions began with a low-intensity warm-up; modality determined by the participant and trainer. Following the warm-up, participants engaged in several stretching and breathing exercises. Movements involved a combination of seated, standing, and mat-based breathing exercises. Maternal HR was continuously monitored to ensure that participants did not exceed light intensity exercise (<40% $VO2_{peak}$).

## Data Collection

Data was collected when the infant was four weeks of age. Before the infant was brought to the 1-month visit, the mother was asked to make sure the infant was fed, diaper changed, and to have napped. These requests decrease the likelihood of agitation, and if the infant becomes too fussy, the data will not be reliable. In other words, the technology used to retrieve the infant's HR, BR, and HRV is sensitive, requiring the infant to be calm for the most accurate recording. Infants, just like other people will show lower HR and BR, and variation between heartbeats (HRV) will be higher when relaxed (Harvard Health, 2021)

The infant's HR changes depending on their activity state (Campos & Brackbill, 1973), therefore I categorized whether the infant was in an active or quiet state at the data collection time. A quiet state was reported if an infant slept, lay still, or had minimal movement. An active state was reported when the infant was excessively moving or crying. These two activity states were stratified when comparing data due to the known influence on measures such as HR, HRV, and BR.

Other maternal and infant characteristics were also recorded. Maternal descriptors included gestational weight gain, maternal age, pre-pregnancy body mass index (BMI), 16-week resting heart rate (HR), 16-week $VO_{2peak}$, parity, maternal race, and exercise compliance. These characteristics were collected via the Balke treadmill test, vo2 max test, informational survey, and weight collection using a digital platform scale. A numerical value for compliance was determined by taking the number of sessions the participants completed week, and dividing by the number of weeks the participant had been training. Infant characteristics included gender, gestational age, infant weight, and infant length and were collected via electronic health records following delivery. All information was kept in and computed by the Redcap system; the online database used for the study.

**Hexoskin Software**

The Hexoskin recording cloud receives data from a Hexoskin smart garment. This garment continuously monitored the infant's cardiorespiratory function by the sensors embedded within the shirt. It is a 1-lead electrocardiogram (ECG) and is equipped with two respiratory inductive plethysmography sensors. During the Hexoskin recording, the Bluetooth device recorded infant average HR (bpm), breaths per minute (BrPM), and RMSSD (ms) values. As previously discussed, HR is the number of times the infants' heartbeats per minute, BR is the number of breaths per minute, and RMSSD is the square root of the mean squared differences of successive R-R intervals. RMSSD was the measure used when assessing HRV in this study due to the recording of measurements lasting only 10 minutes. RMSSD is considered the superior measure of HRV when measuring a short-term duration, and is the primary time-domain measure used to estimate the vagally mediated changes reflected in HRV . The unique and advantageous thing about this test is that it connects via Bluetooth to an app on a cellular phone that records and interprets the data. Before the Hexoskin garment was put on the infant, it was essential to wet the sensors to ensure good conductivity. During this test, it was important for the infant to remain still, so they were either held or placed in their car seat. One challenge we faced for the 1month infants is that even with the smallest Hexoskin shirt, it was still big on the infant. To accommodate, we placed a belt around the garment and infant together, ensuring a snug fit. This belting process was accomplished while keeping the sensors placed in the correct locations.

As previously stated, once the Hexoskin recording started it was important for the infant to remain calm. The infant activity state was reported based on the infant's behavior during this recording. A quiet state was reported if the infant was sleeping, laying still, or minimal movement was observed during the recording. An active state was reported if the infant was excessively moving or crying during the recording. The recording lasted a minimum of 10minutes to ensure enough resting data with minimal abstract data received. When abstract is seen in Hexoskin, it is usually a sign of poor connection in the sensors. Once the data was reviewed on the app and it was determined to be sufficient, the test was stopped. The data was automatically stored in the Hexoskin cloud and available for review.

**Analysis**

To determine the significance of maternal and infant descriptors, one-way analysis of variance (ANOVA) tests were performed for normally distributed variables. These descriptors are as follows; infant heart rate (HR), infant weight, infant length, maternal age, gestational weight gain, and $VO_{2peak}$. Kruskal Wallis tests were performed for the variables that were not normally distributed. These variables are as follows; infant breathing rate (BR), infant RMSSD, gestational age, compliance, pre-pregnancy BMI, parity (the number of times that a woman had given birth), and16-week maternal heart rate (HR).

Regression analyses were done to evaluate the influence of the exercise group on predicting infant HR, RMSSD, and BR; for this test, the exercise group was determined by giving a number based on the increasing intensity of the group activity. For the HR and BR test, we controlled for pre-pregnancy BMI ($kg/m^2$), gestational age (years), and maternal exercise attendance (percent). For the infant RMSSD test, we controlled for gestational age and exercise group.

In addition to the ANOVA comparison to look for differences between the 4 groups, the data were stratified by intent-to-treat protocol, per-protocol, and infant activity state. When comparing the effects of infant gender, a Chi-square test was performed. T-tests were also performed to determine if differences were based on infant gender and stratified by the exercise group to which the mother was randomized. Based on findings, a stratified ANOVA was done based on maternal pre-pregnancy BMI of both normal weight and overweight/obese samples. All tests performed were set to an alpha level of .05 and a power of 95%. All analysis tests were done using IBM SPSS Statistics Version 28.

# Chapter 4: Results

## Study Population

For this study, we collected data from infants using the Hexoskin system. 95 participants participated by bringing their infant in to record these measures. Of the 95 participants that returned for the one-month visit, 19 recordings were excluded due to the Hexoskin system being unable to interpret the data recorded. This resulted in a total of 74 participants in the sample size (14 control, 21 combination, 18 resistance, and 21 aerobic). For all groups, female (F) to male (M) infants ratios were as follows: (control = 4F: 10M, combination = 11F: 10M, resistance = 7F: 11M, aerobic = 10F: 11M).

## Maternal Descriptors

To determine if there were inherent differences between exercise groups, we evaluated maternal characteristics: gestational weight gain, maternal age, pre-pregnancy body mass index (BMI), 16-week resting heart rate (HR), 16-week $VO_{2peak}$, parity, and exercise compliance. Within these measures, there were significant differences in pre-pregnancy BMI; these differences were between the resistance group and the combination group (p=0.01), as well as between the resistance and control (p=0.01) (Table 2).

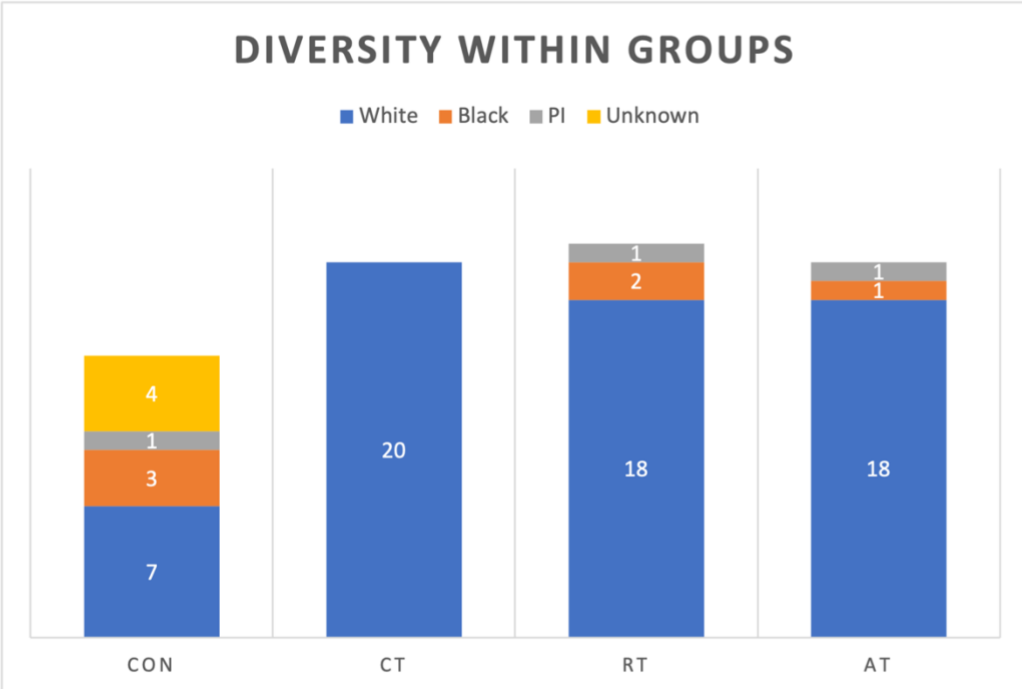
Table 2. Maternal Descriptors (N=74)

| Variables | Control | Combination | Resistance | Aerobic | P Value | Effect Size |
|---|---|---|---|---|---|---|
| Gestational Weight Gain (KG) | 30.37 ± 11.98 | 31.94 ± 10.83 | 34.10 ± 9.25 | 31.16 ± 9.62 | .75 | .02 |
| Maternal Age (Years) | 30.07 ± 4.73 | 30.71 ± 4.22 | 32.39 ± 3.85 | 30.81 ± 4.33 | .45 | .04 |
| Pre-Pregnancy BMI (KG/M^2) | 26.6 (20.5,33.3) | 25.98 (21.03,35.94) | 22.47 (19.58,32.00) | 24.37 (19.79,40.77) | **.03*** | .97 |
| 16-week HR (BPM) | 83 (66,134) | 85 (66,99) | 78 (60,98) | 86.5 (65,108) | .27 | .43 |
| Enrollment VO2 Peak (ml/m/kg) | 1.67 ± .31 | 1.79 ± .31 | 1.66 ± .28 | 1.68 ± .39 | .66 | .03 |
| Parity | 0 (0,2) | 0 (0, 2) | 0 (0,3) | 0 (0,3) | .46 | .06 |
| Total Compliance (Precent) | 0.86 (0,1) | 0.89 (0.49,1.01) | 0.86 (0.51, 1.09) | 0.82 (0.46,1) | .88 | .86 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Mothers' race was not a maternal characteristic evaluated for differences between exercise groups. However, it is important to note the diversity seen within the groups. With noting the diversity, we are able to see if maternal race has any effect on infant outcomes. Table 3 shows the diversity reported within the groups.

Table 3. Diversity Within Groups




*Groups are represented as CON for Control, CT for Combination Training, RT for Resistance Training, and AT for Aerobic Training. The race is represented in the groups by blue for White/Caucasian, Orange for Black/ African American, Grey for Pacific Islanders, And yellow for unreported data.*

**Infant Descriptors**

The infant descriptors collected were as follows: gender, gestational age, infant length, and infant weight (Table 4). These descriptors were used to determine differences between groups. Infants ranged in weight from 2.45 kg to 4.5 kg with an average of 3.6 kg. The infants' length ranged from .41 m to .55 m with an average of .49 m. Also, all infants were delivered at what is considered a full-term pregnancy (36 weeks or more). Table 4 shows that there are no differences between groups regarding these infant characteristics.

Table 4 Infant Descriptors (N=74)

| Variables | Control | Circuit | Resistance | Aerobic | P Value | Effect Size |
| --- | --- | --- | --- | --- | --- | --- |
| **Gender (Percent)** | F:29%; M:71% | F:48%; M52% | F:39% ; M:61% | F:47% ; M: 52% | <.001 | .74 |
| **Gestational Age (Years)** | 39.3 (37,40.9) | 39.6 (37,41.9) | 39.8 (36.7,41.1) | 40 (37.3,41.3) | .64 | .41 |
| **Infant Length (M)** | .50 ± .028 | .496 ± .02 | .49 ± .03 | .492 ± .03 | .48 | .04 |
| **Infant Weight (KG)** | 3.53 ± .49 | 3.54 ± .49 | 3.60 ± .52 | 3.53 ± .496 | .97 | .003 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum). Gender values are represented by percentages of females and males included in that exercise group.*

**Infant Outcomes**

Infant heart and autonomic nervous system outcomes were collected by the Hexoskin system, as has been described, including infant heart rate (HR), RMSSD, and Breathing Rate (BR). These specific variables were used to determine any differences between groups. However, there were none (Table 5). The infant outcomes data were stratified by the intent-totreat protocol, per-protocol, quiet state, and active state. Intent-to-treat protocol included all participants who completed the study and had their infant's Hexoskin measurements recorded. Per-protocol data only included mothers who had 80% compliance or higher with a successful infant Hexoskin recording. A quiet state, as previously stated, was reported if an infant was sleeping, eating, laying still, or minimal movement was seen during the recording. An active state was reported if an infant was excessively fussy, moving, or crying during the recording.

Table 5 Infant Heart Outcomes (N=74)

| VARIABLES | CONTROL (N=14) | CIRCUIT (N=21) | RESISTANCE (N=18) | AEROBIC (N=21) | P VALUE | EFFECT SIZE |
|---|---|---|---|---|---|---|
| HR (BPM) | 148.36 ± 18.05 | 153.24 ± 11.65 | 153.83 ± 13.0 | 149.57 ± 14.76 | .60 | .03 |
| BR (BrPM) | 4.8 (1.9,23.26) | 5.92 (1.85,12.21) | 5.89 (2, 29.87) | 5.68 (2.15, 47) | .84 | .03 |
| RMSSD (MS) | 8.9 (4.75,23) | 8.67 (5.31,26) | 8.47 (3.58, 17) | 9.14 (4.1, 15) | .97 | .02 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

A per-protocol analysis was then done. Only data of participants who completed their exercise intervention at or above 80% compliance were analyzed. After applying the perprotocol criteria, 25 participants were excluded. There are no significant differences between groups (Table 6).

Table 6 Infant Heart Outcomes – Compliance (N=50)

| VARIABLES | CONTROL (N=8) | CIRCUIT (N=15) | RESISTANCE (N=13) | AEROBIC (N=14) | P VALUE | EFFECT SIZE |
|---|---|---|---|---|---|---|
| HR (BPM) | 143± 17.5 | 151.6± 10.3 | 152.08± 10.8 | 145.7± 15.74 | 0.31 | 0.07 |
| BR (Brpm) | 5.11 (1.9,23.26) | 5.92 (1.85,12.21) | 5.86 (2, 29.87) | 5.26 (2.15,11.19) | 0.52 | 0.08 |
| RMSSD (MS) | 9.5 (7.03,23) | 8.67 (.8, 26) | 8.12 (5.08,15) | 9.99 (4.89,15) | 0.55 | 0.04 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

When assessing heart and autonomic measures, it is critical to control for infant activity state: active vs. quiet. Therefore, we stratified the data based on this variable. Table 7 represents the results of the quiet state outcomes; there are no significant differences between groups. For the active state, there are no significant differences between groups (Table 8).

Table 7. Infant Heart Outcomes – Quiet State (N=40)

| Variables | Control (n=5) | Combination (n=12) | Resistance (n=11) | Aerobic (n=12) | P Value | Effect Size |
|---|---|---|---|---|---|---|
| Heart Rate (BPM) | 142.4 ± 17.86 | 152.75 ± 10.76 | 153.45 ± 11.14 | 144.5 ± 15.14 | .20 | .12 |
| RMSSD (MS) | 12 (7.03, 13) | 8.73 (5.42,26) | 8.3 (5.08, 15) | 9.79 (4.89,13) | .89 | .01 |
| Breathing rate (BrPM) | 2.88 (1.9, 5.42) | 5.64 (1.85,12.21) | 5.63 (2, 17.4) | 5.26 (2.15,11.19) | .61 | .04 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Table 8. Infant Heart Outcomes – Active State (N=10)

| VARIABLES | CONTROL (N=3) | CIRCUIT (N=3) | RESISTANCE (N=2) | AEROBIC (N=2) | P VALUE | EFFECT SIZE |
|---|---|---|---|---|---|---|
| **HR (BPM)** | 144 ± 20.66 | 147 ± 7.81 | 144.5 ± 4.95 | 153 ± 24.04 | .93 | .07 |
| **BR (BrPM)** | 4.8 (4.25,21.04) | 5.71 (2, 6.16) | 17.27 (4.66,29.87) | 4.54 (3.36,5.71) | .83 | .32 |
| **RMSSD (MS)** | 10 (8.9,23) | 9.85 (7.6,14) | 8.41 (6.81,10) | 14.5 (14,15) | .35 | .28 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Since initial analysis demonstrated significant differences in maternal pre-pregnancy BMI, we stratified the data based on that variable to determine if it influenced cardiac autonomic outcomes. The reported values of pre-pregnancy BMI were categorized as normal if the BMI value was below 25; above 25 was reported as Overweight/Obese. There are no significant differences in the infant measures based on pre-pregnancy BMI. For that reason, the data is not shown.

Since there were inherent differences in males and females regarding HR and HRV, we also stratified the data based on infant sex. The difference in HR and HRV in adults is thought to be determined by the functional and morphological status of the ANS, cardiovascular system, and hormones. Studies in infants have shown the same pattern as that in adults: male infants have a decreased HR compared to girls (Nagy et al., 2000). The differences between male and female infants with the intent-to-treat sample are shown in Table 9. There are no significant differences between the four treatment groups.

**Table 9. Female vs. Male comparison for 1-month outcomes ITT (intention to treat) (N=75)**

| | CONTROL | | | | COMBINATION | | | | RESISTANCE | | | | AEROBIC | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | Female (n=4) | Male (n=10) | P value | Effect Size | Female (n=11) | Male (n=10) | P value | Effect Size | Female (n=7) | Male (n=11) | P value | Effect Size | Female (n=10) | Male (n=11) | P value | Effect Size |
| HR (BPM) | 162.75± 11.29 | 142.6± 17.3 | 0.06 | 1.3 | 154.27± 12.5 | 152.1± 11.2 | 0.68 | 0.18 | 157.8± 8.7 | 151.3± 14.9 | 0.31 | 0.51 | 148.6± 18.2 | 150.5± 11.7 | 0.78 | 0.12 |
| RMSSD (MS) | 7.95± 3.53 | 10.73± 5.0 | 0.34 | 0.6 | 10.1± 5.9 | 10.29± 6.3 | 0.94 | 0.03 | 8.17± 2.9 | 9.4± 3.9 | 0.48 | 0.35 | 8.0± 3.1 | 9.7± 3.29 | 0.24 | 0.53 |
| Breathing Rate (BrPM) | 7.51± 5.23 | 8.83± 8.05 | 0.77 | 0.18 | 5.9± 3.0 | 5.6± 3.16 | 0.84 | 0.09 | 11.47± 9.2 | 7.33± 7.2 | 0.3 | 0.52 | 9.5± 13.4 | 6.2± 4.01 | 0.44 | 0.34 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Similarly, after stratification for infant sex, we also did a per-protocol analysis to account for compliance above 80% (Table 10). There are no significant difference found between the groups.

**Table 10. Female vs. Male comparison for 1-month outcomes PP (n=53)**

| | Control | | | | Combination | | | | Resistance | | | | Aerobic | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | Female (n=4) | Male (n=7) | P value | Effect Size | Female (n=9) | Male (n=6) | P value | Effect Size | Female (n=6) | Male (n=7) | P value | Effect Size | Female (n=7) | Male (n=7) | P value | Effect Size |
| HR (BPM) | 162.75±11.29 | 139.71±15.67 | **0.03*** | 1.5 | 151.11±11.26 | 152.33±9.54 | 0.83 | 0.12 | 157±9.21 | 147.86±10.84 | 0.13 | 0.9 | 144.14±19.74 | 147.29±11.91 | 0.73 | 0.19 |
| RMSSD (MS) | 7.95±3.53 | 11.86±5.30 | 0.23 | 0.82 | 10.91±6.29 | 9.33±5.01 | 0.62 | 0.27 | 7.7±2.84 | 9.66±2.84 | 0.24 | 0.69 | 9.08±3.07 | 5.52±2.84 | 0.25 | 0.64 |
| Breathing Rate (BrPM) | 7.51±5.23 | 9.08±9.03 | 0.76 | 0.2 | 6.1±2.96 | 6.43±3.56 | 0.85 | 0.1 | 12.39±9.71 | 5.45±2.81 | 0.08 | 1.01 | 4.86±2.68 | 11.1±3.22 | 0.67 | 0.24 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Next, data organized by infant sex was also stratified by quiet and active state. The quiet state data of male vs. females is in Table 11. Active state data is not analyzed due to small sample size. Although there are no significant differences between groups, there are trends with large effect sizes demonstrating that male infants typically have lower resting HR with increased HRV regardless of the exercise group.

**Table 11. Female vs. Male comparison for 1-month outcomes (N=42)**

| | CONTROL | | | | COMBINATION | | | | RESISTANCE | | | | AEROBIC | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | Female (n=3) | Male (n=4) | P value | Effect Size | Female (n=6) | Male (n=6) | P value | Effect Size | Female (n=5) | Male (n=6) | P value | Effect Size | Female (n=7) | Male (n=5) | P value | Effect Size |
| HR (BPM) | 160.67±12.86 | 136.5±13.9 | 0.07 | 0.92 | 153.17±12.78 | 152.33±9.5 | 0.9 | 0.07 | 158.8±9.04 | 149.0±11.42 | 0.16 | 0.94 | 144.14±19.74 | 145.0±6.7 | 0.93 | 0.05 |
| RMSSD (MS) | 8.99±3.49 | 10.28±2.73 | 0.61 | 0.42 | 11.27±7.64 | 9.33±5.0 | 0.61 | 0.3 | 7.88±3.13 | 9.59±3.11 | 0.38 | 0.55 | 9.09±3.07 | 9.7±2.71 | 0.71 | 0.22 |
| Breathing Rate (BrPM) | 7.8±6.4 | 8.37±10.04 | 0.96 | 0.07 | 6.8±3.16 | 6.4±3.56 | 0.84 | 0.12 | 8.88±5.1 | 5.58±3.05 | 0.21 | 0.81 | 4.86±2.68 | 5.91±3.28 | 0.56 | 0.36 |

*Normally distributed variables are represented by mean ± standard deviation. Non normally distributed variables are represented by median and (Minimum, Maximum).*

Regression analyses were performed to identify which variables predict infant autonomic and heart outcomes. Results are shown in Table 12. The infant heart rate variable was controlled for pre-pregnancy BMI, gestational age, exercise group, and exercise compliance. The exercise group descriptor of this test was organized in the order of increasing metabolic equivalents (METS). This test found that the exercise group, meaning the intensity of maternal exercise, predicts infant heart rate (p =.01) with the model and R2 (.15). The infant RMSSD was controlled for the exercise group and gestational age. The results of this test showed that gestational age predicts infant RMSSD (p=.03). There are no significant predictors of infant breathing rate.

**Table 12. Regression Analysis of 1-Month Outcomes**

| Per Protocol Sample (N=69) | | |
|---|---|---|
| **Contributing variables** | **95% CI** | **P Value** |
| **Infant Heart Rate** | | |
| PP BMI | -.29, 1.26 | .22 |
| GA | -4.2, 1.97 | .47 |
| Exercise Group | 1.1, 8.16 | **.01** |
| Compliance | -27.88, 3.3 | .12 |
| **Infant Breathing Rate** | | |
| PP BMI | -.23, .65 | .35 |
| GA | -.91, 2.6 | .34 |
| Exercise Group | -1.73, 2.29 | .78 |
| Compliance | -10.49, 7.23 | .72 |
| **Infant RMSSD** | | |
| Gestational Age | .09, 1.96 | **.03** |
| Exercise Group | -1.4, .82 | .61 |

# Chapter 5: Discussion

I hypothesized that there would be  decreased HR, BR, and increased RMSSD in one-month infants born to mothers who participated in the moderate-intensity exercise groups compared to the infants of women in the control group. The primary findings of this study demonstrate exercise type, intensity, predict one-month infant HR. Further, the data suggest male infants have more mature cardiac autonomic nervous system compared to female counterparts. The findings showed no significant differences between the exercise groups. After controlling for infant activity state, there still were no significant differences between groups.

Although there were no significant findings for one-month outcomes between groups, regression analysis did show that the exercise group– in the order of increasing intensity– predicts resting infant HR. This result further supports the idea of a dose-response relationship with exercise. Similar results were found by May et al., (2010), who looked at 36-week data from MCG recordings and activity questionnaires. They discovered that maternal exercise intensity and energy expenditure have a dose-response effect on the fetal heart.

A different study conducted by May et al. that looked at 1-month infants discovered significance in infant RMSSD for women who were a part of the exercise groups (2014a,). Contrasting results were found when comparing the study by May et al. and this study regarding infant RMSSD. May et al. used Magnetocardiography, while this study used a Hexoskin smart garment. Both devices are an accurate non-invasive way to retrieve infant HRV. Results could differ due to different types of technology being used to retrieve RMSSD values. A challenge our study faced using the Hexoskin shirt was ensuring a snug fit on the baby. Using the smallest size available often was still big on the infant.

Winn et al., (1994) found decreased fetal breathing rate after maternal aerobic exercise. Our study did not come to the same conclusion. The difference in findings could be due to differences in the population of each study. Winn et al. had 12 participants, while this study had data for 74 participants. Although they found significance in decreased fetal breathing rate, a smaller sample size increases the likelihood of significance being due to chance.

Our study found no significant differences comparing male to female heart outcomes but did find trends with large effect sizes. These large effect sizes demonstrate that male infants have increased HRV and lower resting HR, indicative of more mature autonomics than their female counterparts. (Nagy et al., 2000) found similar results when comparing gender-related differences in HR of human neonates. Their study found that newborn male infants have lower baseline HR than newborn females. The gender-related differences in HR in infants are also seen in the adult population. Therefore, this phenomenon is thought to already be present at birth and persist throughout life.

Our study did not show which exercise best affects infant heart outcomes, but it does show that different modes of gestational exercise are safe to perform. The results showed that one-month-old infants exposed to any type of exercise have similar HR, HRV, and BR relative to infants of non-exercisers. We also found that exercise, specifically the intensity level, predicts infant resting HR. This is an additional step toward understanding what influences the infant's cardiac autonomic nervous system. A more mature cardiac autonomic nervous system has the potential to reduce future CVD risk, improving public health outcomes. Based on these findings, we recommend that healthcare providers continue encouraging women to exercise at moderate intensity while pregnant. Although the outcomes in this study provide justification for exercise during pregnancy, more research is necessary to fully understand the infant cardiac autonomic nervous system outcomes.

**Strengths:**

There are several strengths to recognize regarding this study, including: 1) it was a randomized controlled exercise intervention trial; 2) the exercise was supervised; 3) attendance was tracked; 4) the intensity was monitored to meet recommended levels; and 5) it was completed throughout the second and third trimesters of pregnancy.

**Limitations**:

There are limitations to consider when interpreting the results of this study. One limitation was that the sample size of the study was small. With a power of 95%, either a sample of 120 total participants– or 40 participants per group– was needed. We were unable to reach this target. When completing a study of this length (enrollment phase to completion being roughly ten months), it can be challenging to obtain all of the measures. For example, 52 participants who completed the study did not return for the one-month infant measures. This lack of full participation could relate to: mothers not wanting to proceed with infant measurements after delivery, mothers moving out of the area, or scheduling-conflicts. Additionally, the sample sizes decreased once we accounted for the per-protocol analysis and stratified based on infant activity state. With sample sizes being small for each group, slight differences in measures could cause a significant impact on the overall data set and statistical outcomes.

Another potential limitation in this study was the Hexoskin shirt needing to fit snuggly to get a good recording. Even when using the smallest size available for the one-month measures, this obstacle was still challenging to overcome fully. Because of this issue, some data could not be used for the analysis.

Lastly, a potential limitation was that our control group performed light intensity exercise instead of no exercise. Based on previously reported research, there is a dose-response relationship with exercise (May et al., 2012). Since we used a stretching/yoga protocol in this study to retain participants, the light intensity for the control group may be diluting the potential differences of the moderate intensity exercise groups.

## Future Research Directions

Besides the obvious benefit of a larger sample size in statistical analysis, including more measurements at the one-month infant visits would be beneficial. Including cardiac output and ejection fraction measures would allow a more in-depth look at the infant cardiac autonomic systems development. Using different types of instrumentation, such as echocardiograms, would be a way to examine the infant's heart function. Looking at the infant's past one month would also be essential to see if these changes persist with age. With these additions, it would be interesting to see the impact different maternal exercise intensities have on infants' cardiac autonomic nervous system.

## Conclusion

This study data showed interesting trends. Notably, any exercise type or stretching is safe during pregnancy based on infant cardiac and autonomic health measures. Further, the data suggest that one-month-old infants exposed to any type of exercise have similar HR, HRV, and BR relative to infants of non-exercisers. As well, exercise type and specifically intensity, predicts infant resting HR with a dose-response relationship.

This study does not prove that moderate-intensity exercise results in an infant's more mature cardiac autonomic nervous system. Although the large effect sizes found demonstrate that male infants have increased HRV and lower resting HR, indicative of more mature autonomics than their female counterparts. Further research will need to be done with a larger sample size to better understand the relationship between pre-pregnancy BMI, gestational age, exercise group, and infant gender on infant heart outcomes. That future research will invite a better understanding of how maternal moderate intensity exercise affects the infant cardiac autonomic nervous system. Application of that knowledge could decrease the chance of developing CVD risk factors before birth and thus ideally prevent unnecessary deaths in the next generation.

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Appendix

**EAST CAROLINA UNIVERSITY**
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600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914** · Fax **252-744-2284** ·
**rede.ecu.edu/umcirb/**

## Notification of Amendment Approval

| | |
|---|---|
| From: | Biomedical IRB |
| To: | Linda May |
| CC: | Ashland Haire |
| Date: | 8/3/2022 |
| Re: | Ame55_UMCIRB 12-002524<br>UMCIRB 12-002524<br>ENHANCED by Mom |

Your Amendment has been reviewed and approved using expedited review for the period of 8/2/2022 to 12/19/2022. It was the determination of the UMCIRB Chairperson (or designee) that this revision does not impact the overall risk/benefit ratio of the study and is appropriate for the population and procedures proposed.

Please note that any further changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. A continuing or final review must be submitted to the UMCIRB prior to the date of study expiration.The investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).

The approval includes the following items:

| Document | Description |
|---|---|
| Changes to Study Team/Personnel - addition of Stancell, Grantham, McLaurin, and Kern | |

For research studies where a waiver or alteration of HIPAA Authorization has been approved, the IRB states that each of the waiver criteria in 45 CFR 164.512(i)(1)(i)(A) and (2)(i) through (v) have been met. Additionally, the elements of PHI to be collected as described in items 1 and 2 of the Application for Waiver of Authorization have been determined to be the minimal necessary for the specified research.

The Chairperson (or designee) does not have a potential for conflict of interest on this study.