PAAH
PHYSICAL ACTIVITY AND HEALTH

Gao, Y., et al. (2020). Impact of Physical Activity During Pregnancy on Gestational Hypertension. *Physical Activity and Health,* 4(1), pp. 32–39. DOI: https://doi.org/10.5334/paah.49

REVIEW

Impact of Physical Activity During Pregnancy on Gestational Hypertension

Yajie Gao[1], Shuaijun Ren[1], Huanzhen Zhou[2] and Rongrong Xuan[2]

[1] School of Medicine, Ningbo University, Ningbo, CN

[2] Obstetrical Department, The Affiliated Hospital of Medical School of Ningbo University, Ningbo, CN

Corresponding author: Rongrong Xuan (lindapeimin@foxmail.com)

Background: Hypertensive disorders of pregnancy are characterised by new onset of hypertension after 20 weeks gestation, proteinuria and other associated complications, which are major causes of adverse maternal and neonatal outcome. The benefits of physical activity on reducing the risk of essential hypertension, coronary atherosclerotic heart disease and type 2 diabetes are well documented, but the effcet of physical activity on gestational hypertension is inconclusive. This review presents the state of knowledge related to the impact of physical activity on gestational hypertension.

Methods: We searched physical activity and gestational hypertension studies and highlight key articles with a focus on maternal health outcomes to best inform physical activity promotion efforts.

Results: Physical activity during pregnancy can reduce the risk of gestational hypertension by improving placental blood flow perfusion deficiency, reducing oxidative stress, improving insulin resistance and improve the prognosis of maternal and fetus.

Conclusion: Physical activity is of great benefit to improve the occurrence and development of gestational hypertension. Pregnant women should be guided according to individual factors and complications during pregnancy. However, there have no gold standard about physical activity norms based on gestational hypertension. Scientific computation of big data in real-world clinical research are needed in future research.

Keywords: gestational hypertension; preeclampsia; physical activity; pathophysiology

1. Introduction

Hypertensive disorders of pregnancy are common pregnancy-associated disease, mainly manifested as hypertension and damage to important organs such as heart, kidney, liver and nervous system, with the incidence of 5% to 8% (Jim and Karumanchi 2017; Lo et al. 2013). The previous study has proven 16% of maternal deaths can be attributed to gestational hypertension, so it has become an urgent obstetric crisis (Anna et al. 2018). The current therapy of gestational hypertension include antispasmodic, antihypertensive, sedative and termination of pregnancy, all of them are symptomatic treatments after the onset, without safe and effective precaution (Abalos 2001; Amaral et al. 2017). The benefits of physical activity on health, such as reducing the risk of essential hypertension, coronary atherosclerotic heart disease, and type 2 diabetes are well documented, but there is a gap between physical activity and the risk of gestational hypertension (Coenen 2018; Hermann et al. 2014). If it proves to be effective, maybe physical activity can be used as an adjunct and preventive intervention for gestational hypertension. This review is about the impact of physical activity on gestational hypertension.

2. Impact of physical activity on the pathophysiology of gestational hypertension

2.1. Uterine-placental Blood Flow

During pregnancy, the physiological changes of the uterine vessels in the early and mid-pregnancy period are manifested as "vascular remodeling". The high exhaustion and low resistance of the uterine arteries are essential to maintain adequate placental blood perfusion. As the pregnancy progresses, the resistance

of uterine spiral artery blood flow was decreased gradually, the V-shaped notch in early diastole tends to be flat and even disappear in late pregnancy. Preeclampsia has uterine-placental and placental-fetal blood flow perfusion disorder, which is manifested by resistance of the uterine arteries and umbilical arteries is increased and blood supply is reduced. These physiological changes lead to placental perfusion reduced and hypoxia, causing immune activation, oxidative stress and endothelial dysfunction. If placental function is impaired, it will cause intrauterine growth retardation. In severe cases, spiral arterial embolism, decidual necrosis and bleeding can occur, leading to adverse pregnancy outcomes such as placental abruption (Asnafi and Hajian 2011).

Studies have found that exercise training before and during pregnancy can attenuate the development of placental ischemic-induced hypertension, angiogenic imbalance and oxidative stress in rat (Gilbert et al. 2012). In addition, regular exercise training in the second half of pregnancy can increase the expression of eNOS and NO production and decrease the generation of reactive oxygen species in human placenta (Ramírez-Vélez et al. 2013). This adaptation may contribute to the beneficial effects of exercise on the vascular and antioxidant system, and then reduce the risk of preeclampsia.

An early human study showed that exercise during the last trimester of pregnancy resulted in reduced uterine blood flow and a greater reduction in patients with preeclampsia, providing the reasons that gestational hypertension women should rest on bed or reduce activity (MORRIS 1956). Nevertheless, pregnancy is a hypercoagulable state, prolonged bed rest will increase the risk of venous thrombosis. In recent years, the impact of physical activity during pregnancy on uterine-placental blood flow perfusion has caused widespread concern among scholars. Szymanski et al. found that the mean uterine artery Doppler indices (pulsatility index, resistance index, systolic/diastolic ratio) did not significantly change during moderate-intensity exercise (40–59% of heart rate reserve) according to the exercise guidelines of pregnant women, which indicates that after routine exercise, uterine arterial blood flow is not reduced (Szymanski and Kogutt 2018). However, after vigorous-intensity exercise (60–84% of heart rate reserve), all mean uterine artery Doppler indices showed reductions, which may cause decreased in uterine blood flow and may adversely affect fetal health. This shows that the impact of physical activity during pregnancy on uterine artery blood flow is closely related to exercise intensity.

In addition, some studies have found that regular physical activity during pregnancy increases the rate of placental bed blood flow, which may be related to the increase of fetal-placental oxygen transport. Regular exercise during pregnancy increases villous vascular development and cell proliferation, and increased villous vascular volume improves placental growth by enhancing placental transfer of oxygen and diffusible substrates (Bergmann et al. 2004). In the first trimester of pregnant, adding a lot of moderate-intensity exercise (60 minutes per day, 5 days per week) will stimulate placental growth, but when the exercise intensity was reduced to lower level (5 times per week, 20 minutes each time) will haven't similar effect (Committee Opinion No. 650 Summary 2015). Clapp found that maternal weight-bearing exercises (such as running, aerobics, cross-country skiing, etc.) from early pregnancy can increase the volume and growth rate of the placenta, the proportion of non-functional tissue in the placenta reduced and the functional volume increased, which is conducive to increase the nutrition and gas exchange between fetus and maternal, thereby reducing the maternal-fetal complications associated with preeclampsia (Clapp 2003).

2.2. Cardiovascular System

In order to adapt the needs of pregnancy and fetal growth, the cardiovascular system undergoes a series of changes, such as increased blood volume, cardiac output, blood coagulation content and decreased vascular tone. Decompensation of cardiovascular system can cause hypertensive disorders of pregnancy. Before the onset of clinical symptoms of preeclampsia, the cardiac output was increased, and the systemic vascular resistance was not significantly different from that of normal pregnant women. After the onset of clinical symptoms of preeclampsia, the cardiac output was decreased, and the systemic vascular resistance was increased, resulting in myocardial ischemia, reduced myocardial contractility, ventricular function is highly dynamic and endothelial cell activation increases vascular permeability. Endovascular fluid enters the interstitial cell will cause interstitial edema, myocardial point bleeding or pulmonary edema, even cause heart failure in severe cases (Paauw et al. 2018; Basky et al. 2019).

Acute exercise will increase the production of pro-oxidants, and the corresponding consumption of antioxidants is needed to restore oxidative balance (Jason et al. 2018). When physical activity is repeated regularly, human body will adapt by strengthening the antioxidant defense system to limit the cellular damage caused by exercise-induced oxidative stress. Regular exercise can increase superoxide dismutase and glutathione peroxidase in skeletal muscle, plasma and liver, up-regulate antioxidant capacity, and may

reduce oxidative stress leading to endothelial dysfunction in preeclampsia (Powers et al. 1999; Paschalis et al. 2018). Aerobic regulation can also increase the number of mitochondria in the muscle, thereby increasing the body's resistance to oxidation. Yeo et al. found that in pregnant women at risk of preeclampsia, moderate exercise for 10 weeks (18–28 weeks of pregnancy) can significantly reduce diastolic blood pressure (Yeo et al. 2000). The reduction may be due to the effects of exercise itself, not weight or overall daily physical activity levels. In addition, studies have confirmed that light-intensity aerobic exercise and strength training during pregnancy had no significant effect for echocardiographic variables, Cerebrovascular Disease (CVD) risk factors, type of labor, or newborn's outcomes (weight, height, head circumference, Apgar scores, and umbilical cord pH) (Perales et al. 2015). It means that light-intensity aerobic exercise is safe for healthy pregnant women and does not cause additional cardiac overload or affect major pregnancy outcomes beyond gestation. A prospective case-control study included 24 normotensive preeclampsia women and 20 healthy women assess the impact of 12 weeks of exercise training (70–80% maximum oxygen utilization) in preeclampsia women improves components of MetS, endothelial function, vascular wall thickness and autonomic control. However, trained women with preeclampsia can only achieve a cardiovascular status comparable to sedentary healthy controls (Narvaez-Sanchez et al. 2014).

2.3. Insulin Resistance

Pregnancy is characterized by adaptive changes in physiology, endocrine and metabolism, thereby forming a pseudodiabetic state of progressive insulin resistance. These changes occur to allow glucose and lipids to be transferred to the developing fetus and to maintain the fetus' continuing need for nutrition and oxygen. Insulin resistance is usually related to gestational hypertension, which pathogenesis includes endothelial dysfunction, angiotensin receptor overexpression, increased renal reabsorption of sodium, etc. Gestational hypertension make insulin resistance aggravate, the vicious circle of the two poses cause great threat to the health of pregnant women and fetus.

Insulin resistance develops at the level of skeletal muscle, and its chronic activity or disorder accordingly releases muscle factors that regulate insulin sensitivity and cardiovascular adaptation through direct or indirect mechanisms. In non-pregnant women, the strength and quality of skeletal muscle is inversely related to the occurrence of insulin resistance. In pregnant women, muscle activity regulates metabolism and vascular adaptation (Raul et al. 2019). Physical activity, especially exercise involving large muscle groups, can improve glucose tolerance and insulin sensitivity, reduce the risk of gestational hypertension and improve the prognosis. Studies have shown that the improvement of insulin sensitivity related to exercise training is related to changes in the expression and activity of proteins involved in insulin signal transduction in skeletal muscle (such as AMPK, PI3K, AKT and IRS, etc.) (Henriksen 2002). In addition, increased lipid oxidation and metabolism may be another mechanism by which exercise improves insulin sensitivity: exercise training leads to increased skeletal muscle oxidation by increasing lipid oxidation and mitochondrial-related protein expression (Kovo et al. 2017).

3. Intervention of physical activity on the progression of gestational hypertension

Hypertensive disorders of pregnancy often lead to adverse pregnancy outcomes, of which preeclampsia accounts for 15% of preterm birth, increased maternal and fetus morbidity and mortality (Laura et al. 2018). In addition, preeclampsia can lead to maternal risk of long-term CVD, and significantly increase chronic diseases risk such as hypertension, stroke, diabetes, and obesity in offspring (Parikh et al. 2020). The risk of cardiovascular events in preeclampsia is about twice as high as normal blood pressure pregnant women. It turns out that regular physical activity can bring significant benefits to pregnant women and fetus. Maternal benefits include improving cardiovascular function, lightening weight gain in pregnancy (Melzer et al. 2010), mitigating musculoskeletal discomfort, reducing incidence of muscle spasms and lower limb edema, reducing risk of hypertension-related complications (Dempsey et al. 2004; Blaize et al. 2015). Fetal benefits include reducing fat content, improving stress tolerance and promoting nerve development (Harrod et al. 2014; Marques et al. 2015).

Epidemiological studies have shown that physical activity during professional and leisure time is associated with a lower incidence of preeclampsia. Weissgerber indicated that regular physical activity can prevent preeclampsia by intervening in three key stages of the development of hypertension during pregnancy (Weissgerber et al. 2004). (1) Stimulating placental growth and blood supply, improving placental perfusion and transport to prevent reduced fetal substrate and oxygen supply (Roberts and Lain 2002; Salafia et al. 2006). (2) Reduce the oxidative stress of endothelial dysfunction caused by preeclampsia, and up-regulate

antioxidant capacity (Powers et al. 1994). (3) Reverse maternal endothelial dysfunction, prevent gradual deterioration of endothelial function, and reduce secondary maternal symptoms (Laughlin 1995). Research by Sorenson found that moderate-intensity recreational activities during the first 20 weeks of pregnancy reduced the risk of preeclampsia by 24%. Exercising during this period reduced the risk of preeclampsia by 54%, suggesting a dose-response relationship (Sorensen et al. 2003). A published study evaluated the correlation between other types of physical activity (such as housework) and the risk of preeclampsia (Cohen et al. 2015). The study found that women who spent 4 or more hours of household chores each week had a significantly reduced risk of preeclampsia by 60% compared with women with less than 4 hours. For jobs that require more time standing, manual labor, or operating industrial machinery, the tendency to reduce risk is not obvious. In contrast, women with heavy workloads have a slightly increased risk of preeclampsia. This shows that preeclampsia risk is closely related to physical exertion, and not necessarily positively correlated. A prospective birth cohort study associations between occupational characteristics and hypertension during pregnancy in 4465 pregnant woman from early pregnancy onwards in the Netherlands, the result shows no consistent associations between the work-related risk factors, such as long periods of standing or walking, heavy lifting, night shifts, and working hours, nor exposure to chemicals with hypertension during pregnancy. The findings in this study corroborates that a link between physically demanding work and hypertension during pregnancy is insufficient to propose restrictions in activities during pregnancy (Bonzini et al. 2007).

Currently, a large number of studies on the treatment of hypertensive disorders of pregnancy have focused on preventive therapies, including research on antioxidants, calcium supplements and antiplatelet drugs, without much success (Poston et al. 2006; Levine et al. 1997). For this reason, efforts must be made to control the progression of the disease in order to prolong pregnancy. Physical activity maybe can be used as an adjunct and preventive intervention for gestational hypertension.

4. Recommendations for physical activity of gestational hypertension

Aerobic exercise and resistance exercise are commonly exercise methods during pregnancy. Aerobic exercise can improve the cardiopulmonary function of pregnant women, prevent chronic diseases and excessive body mass growth (Ramírez-Vélez et al. 2011; Hegaard et al. 2007; Haakstad and Bø 2011). Aerobic exercise is an effective non-pharmacological and low-cost strategy for reducing blood pressure (Whelton et al. 2002).During pregnancy, aquatic exercise program can decrease maternal discomfort, enhance physical functioning and improve health (Smith and Michel 2006). Brisk walking, when compared with no walking at all, can reduce the risk of preeclampsia by 30% to 33%. Stair climbing was inversely proportional to the risk of preeclampsia (Sorensen et al. 2003). Some articles indicated that yoga can significantly reduce hypertension-related complications, the results suggest yoga to be a safe and effective intervention in high-risk pregnancy during pregnancy (Rakhshani et al. 2012; Jiang et al. 2015). A meta-analysis has shown that aerobic exercise during pregnancy for approximately 30 to 60 minutes twice a week, compared with sedentary can significantly reduce the overall risk of hypertension and cesarean section during pregnancy (Elena et al. 2017). While it is worth noting that preeclampsia was listed as a contraindication to aerobic exercise during pregnancy according to ACOG (American College of Obstetricians and Gynecologists) guildline in 2015.

Resistance exercise focuses on strengthening muscle strength, improving overall health and energizing pregnant women. A randomized controlled trial showed that compared to the aerobic and non-exercise women groupduring pregnancy, the prevalence of hypertension disease and gestational diabetes mellitus (GDM) in the resistance exercise and aerobic exercise group was significantly reduced (White et al. 2014), pre-pregnancy BMI is the most critical factor. Although benefits of resistance exercise are well known, but pregnant women are advised to proceed carefully, especially at moderate to high intensity, which need to be supervised (Petrov et al. 2015).

Refer to clinical guidelines for gestational hypertension in recent years, ISSHP (International Society for the Study of Hypertension in Pregnancy), QLD (Queensland, Australia), SOGC (Society of Obstetricians and Gynaecologists of Canada), SOMANZ (Society of Obstetric Medicine of Australia and New Zealand) and ACOG all recommend exercise as an effective intervention to prevent hypertensive disorders of pregnancy for normal pregnancy (see **Table 1**) (Brown et al. 2018; Guidelines QLD 2016; Magee et al. 2014; Lowe et al. 2014; American College of Obstetricians and Gynecologists. 2013). According to ACOG guidelines in 2013, moderate exercise has been hypothesized to stimulate placental angiogenesis and improve maternal endothelial dysfunction.

For high-risk groups of gestational hypertension, reasonable exercise under the guidance of professionals during pregnancy may be a cost-effective option. The exercise program depends on the type, frequency, intensity, and duration of the exercise, as well as the point in time when women are pregnant during the

Table 1: Exercise recommendations based on guidelines for gestational hypertension.

Hypertensive disorders of pregnancy Guidelines	Recommendations
ISSHP (2018)	Pregnant women should exercise at least 3 days per week for an average 50 min using a combination of aerobic exercise, strength and flexibility training.
QLD (2016)	Advise women will benefit from exercising regularly.
SOGC (2014)	Exercise for maintenance of fitness (I-A) is recommended in pregnancy. Periconceptual and ongoing use exercise (II-2B) may be useful in preventing preeclampsia.
SOMANZ (2014)	Recommend women who have had preeclampsia counsell doctors that they will benefit from exercising regularly.
ACOG (2013)	Thirty minutes of moderate exercise on most days is currently recommended during normal pregnancy.

exercise. However, some types of sports are at risk of being hit and falling, such as skiing, basketball, rugby, horse riding, gymnastics are not recommended. It must be noted that if pregnant women have the following conditions, such as vaginal bleeding, dizziness, headache, chest pain, muscle weakness, premature delivery, reduced fetal movement, premature rupture of membranes, calf pain or swelling, difficulty breathing, it is recommended to stop exercise immediately, stabilize the maternal and fetus as soon as possible. Pregnant women should not exercise again until stabilized.

5. Conclusion

In recent years, a large number of overweight or elderly maternal choose to re-pregnate, leading to an increased incidence of gestational hypertension. In addition to drug intervention, early lifestyle intervention may be a safer preventive measure for gestational hypertension. Physical activity is of great benefit to improve the occurrence and development of gestational hypertension. Early intervention and prevention of hypertensive disorders of pregnancy from pathophysiological mechanisms, such as improving placental blood flow perfusion deficiency, reducing oxidative stress, and improving insulin resistance, will improve the prognosis of maternal and fetus. However, on the premise of ensuring the safety of maternal and fetus, pregnant women should be guided according to individual factors such as the body weight, nutritional status, pre-pregnancy exercise rules, and complications during pregnancy.

At present, there have no gold standard about physical activity norms and recommendations based on gestational hypertension. Future research and interventions should based on theory and include proven and reliable measures, scientific computation of big data in real-world clinical research are needed. We need further research to integrate the effects of physical activity on promoting gestational hypertension before, during, and after pregnancy.

Funding Information

Zhejiang Province Medical and Health Science and Technology Plan Project (2018KY710). Ningbo Public Welfare Science and Technology Plan Project (2019C50095).

Competing Interests

The authors have no competing interests to declare.

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How to cite this article: Gao, Y., Ren, S., Zhou, H., & Xuan, R. (2020). Impact of Physical Activity During Pregnancy on Gestational Hypertension. *Physical Activity and Health,* 4(1), pp. 32–39. DOI: https://doi.org/10.5334/paah.49

Submitted: 12 February 2020 **Accepted:** 07 March 2020 **Published:** 15 April 2020

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