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Pregnancy and insulin sensitivity in relation to Exercise training (A scoping review)

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Abstract: **This study is aimed to estimate the relation of exercise training on insulin sensitivity and pregnancy. Twenty females at the second trimester of pregnancy participated in this study. Their age was 20 to 40 years with BMI less than 35 km^2. They divided into two equal group. The study group (A) performed exercise program for four weeks, 3 sessions per week. While the control group maintain their daily life activity routine. There was a significance difference in the mean value of insulin sensitivity level in group A and there was a significance difference in the mean value between groups in favoring to group (A). So, it could be concluded that exercise training is an effective method on insulin sensitivity during pregnancy.**

Keywords: **pregnancy , insulin senstivity , exercise training.**

LITERATURE REVIEW

Insulin sensitivity is a physiological condition where the natural hormone, insulin, becomes less effective at lowering blood sugars. The resulting increase in blood glucose may raise levels outside the normal range and cause adverse health effects. Certain cell types such as fat and muscle cells require insulin to absorb glucose, when these cells fail to respond adequately to circulating insulin, circulatory glucose levels increase. The liver helps regulate glucose levels by decreasing its secretion of glucose in the presence of insulin. This normal reduction in the liver's glucose production may not occur in people with IR. **(Embaby et al, 2016).**A reduced tissue response to the effect of insulin on glucose metabolism, including a reduced glucose uptake in muscles and fat tissue, reduced liver glycogen formation and accelerated liver glucose production. ***(Maghbooli et al, 2007)*** In early pregnancy, insulin secretion increases, while insulin sensitivity remains the same, decreased, or may even be raised ***(Gomaz et al, 2008)***

Decreased insulin sensitivity or increased insulin resistance is decreased biological response of a nutrient to a given concentration of insulin at the target tissue, e.g. liver, muscle, or adipose tissue.The resistance to insulin can be characterized as pre-receptor (insulin antibodies), receptor (decreased number of receptors on the cell surface), or post-receptor (defects in the intracellular insulin signaling pathway). ***(Catalano, 2016)***

In pregnancy, the decreased insulin sensitivity is best characterized as a post-receptor defect resulting in the decreased ability of insulin to bring about SLC2A4 (GLUT4) mobilization from the interior of the cell to the cell surface. Although human placental lactogen has often been cited as the cause of the decreased insulin sensitivity of pregnancy, because of its production from the placenta and increasing concentrations with advancing gestation, more recently the role of cytokines and elevated lipid concentrations in pregnancy have been correlated with the longitudinal changes in insulin sensitivity in nonpregnant women as well as in pregnant women ***(Catalano, 2016)*** It is associated with an increased maternal risk for other pregnancy-related complications, such as pre-eclampsia, postpartum hemorrhage, abortion rate and with an increased risk for developing type 2 diabetes postpartum .***(Embaby et al,2016)***

Insulin resistance may occur in patient with acromegaly, Cushing's syndrome, history of neonatal mortality or previous cesarean section, maternal age (>35 years). ***(Xiong et al, 2011)***. Obesity is the most common risk factor correlated with decreased insulin sensitivity. ***(Catalano, 2016)***

Gestational diabetes is also put the infant at risk of macrosomia, jaundice and birth trauma. Later in life, children of gestational diabetic mothers have an increased risk for obesity, abnormal glucose tolerance, and type 2 diabetes. ***(Embaby et al, 2016)***

Nutrition of the fetus is mainly supplied by maternal metabolism. In this manner, during normal pregnancy, insulin resistance develops and assists in the provision of energy substrate for the baby.This insulin resistance leads to higher levels of glucose and free fatty-acids, constrained by increased secretion of maternal insulin. In 2–4% of people, the pancreatic insulin response is inadequate and gestational diabetes ensues. ***(Topol and Lauer, 2003)***

Through the span of pregnancy insulin action changes. At 12–14 weeks' gestation, insulin sensitivity is slightly increased but then declines for the rest of the pregnancy, with insulin resistance being highest late in the third trimester. Insulin sensitivity rebounds with delivery of the placenta. Thus gestational diabetes typically obvious late in the second trimester and clears immediately postnatal. ***(Topol and Lauer, 2003)***

Pregnancy is the period that shows a marked and intense changes in the mother's anatomical, hormonal and metabolic status, ***(kirwan et al., 2002)*** which exert significant effects on a woman's body. ***(Motosko et al, 2017)*** that affect many organs and systems ***(Chandraharan and Arulkumaran, 2012)***

These changes to nurture and accommodate the developing fetus are necessary to help the woman to adjust to the pregnant state and to aid fetal growth and survival. ***(Chandraharan and Arulkumaran, 2012)***

Pregnancy is a remarkable biological process involving simultaneous changes in many physiological systems to support the development of healthy progeny. To conserve the health of both the mother and the infant these changes include hormonal changes, weight gain, immune system modulation, and others, must be all synchronized.

While some of the pregnancy-associated hormonal and metabolic changes have been known for decades, the dramatic changes in microbiome composition which is taking place during pregnancy have only recently been appreciated. ***(Ohayon et al., 2016)***

During pregnancy, physiological anatomical changes occur. Which affect the musculoskeletal system both at rest and during exercise ***(FIERIL et al., 2015)***. Weight gain is the most obvious change, which can increase pressure on joints, especially the knees, causing discomfort for joints and damage increase in those previously unstable.

Lordosis and posture changes are obvious, due to the weight gain and increased abdominal volume, putting the pregnant women at risk of balance loss and falls. ***(Biase et al, 2009)***

Eventually, during gestation, increased level of estrogens and relaxin lead to an increased ligament laxity, which may predispose women to a higher risk of tearing and sprain. Although there is no evidence of increased musculoskeletal injury during pregnancy, this incident must be studied when prescribing physical exercise. ***(Biase et al, 2009)***

Cardiovascular and hematological changes occur early as 4 weeks' gestation and are progressive. During pregnancy, the plasma volume increases by 45%. This increase is mediated by the direct action of progesterone and estrogen. This leads to renal sodium retention and an increase in total body water. Through an increase in renal erythropoietin production, red cell mass increases by 20%. As the increase in red cell mass is relatively lesser than that of plasma volume, the hemoglobin falls from 150 g liter–1 pre-pregnancy to 120 g liter–1 during the third trimester. This is termed the physiological anemia of pregnancy. ***(Heidemann and McClure, 2003)***

Increased levels of circulating estrogen and progesterone cause vasodilatation and a consequent fall in peripheral vascular resistance by 20%. As a result, systolic and diastolic blood pressure fall and there is a reflex increase in heart rate of 25%. Stroke volume is increased by 25% and together with that in heart rate, increases cardiac output by 50% by the third trimester. ***(Heidemann and McClure, 2003)***

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The enlarging uterus can compress both the inferior vena cava and descending aorta in the supine position. Compression of the vena cava reduces venous return and results in decreased cardiac output, blood pressure and hence placental perfusion.

Compression of the descending aorta also leads to a reduction in uterine blood flow. This may cause fetal distress. After 20 weeks gestation aortocaval compression typically occurs but must be regarded as the reason for maternal hypotension from the end of the first trimester onwards. To compensate for the effects of aortocaval compression, all pregnant patients should either be turned to the left or have a wedge under their right hip when being positioned supine and the full lateral position utilized as much as possible. ***(Heidemann and McClure, 2003)***

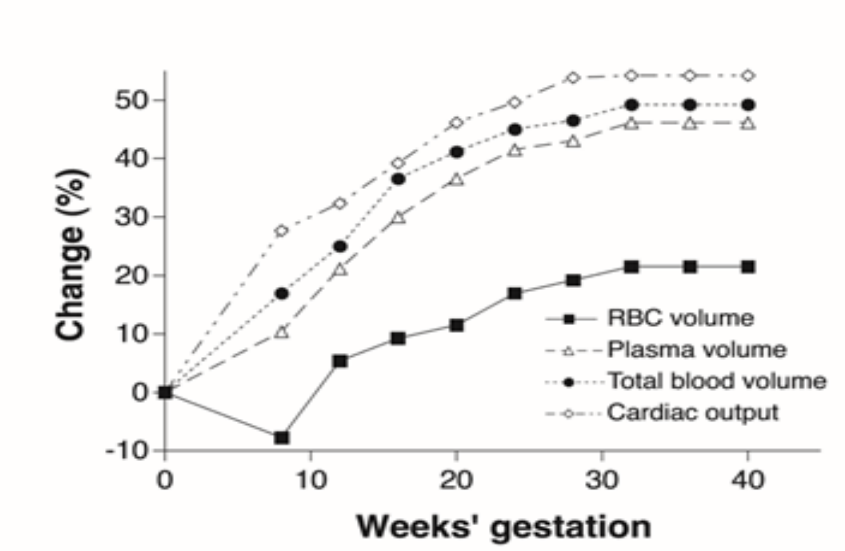

Fig (1): Hematological changes.

Changes in the respiratory system may be classified as anatomical and physiological. Capillary engorgement and edema of the upper airway down to the pharynx, false cords, glottis and arytenoids, they consider as anatomical changes. These changes are important to the anesthetist as edema in the airway makes upper airway obstruction, bleeding more likely during mask anesthesia and may make tracheal intubation more difficult. May be require a smaller diameter of endotracheal tube. ***(Heidemann and McClure, 2003)***

The diaphragm is progressively displaced cranially by the gravid uterus. Minute ventilation rises during pregnancy because there is increase in the diameter of the chest of pregnant women. However, diaphragmatic movement is reduced in late trimester of pregnancy, particularly in the supine position. Also, there is a 20% reduction in functional residual capacity due decreases in both residual and expiratory reserve volumes. ***(Heidemann and McClure, 2003)***

Many of the physiological changes in the respiratory system are mediated by increased progesterone levels, such as bronchial and tracheal smooth muscle relaxation. ***(Heidemann and McClure, 2003)***

Renal plasma flow and glomerular filtration rate during pregnancy increase and that might be expected from the increase in cardiac output. Plasma concentration is lesser in pregnant women compare to non-pregnant due to increase in urea, creatinine, urate clearance and excretion of bicarbonate. The activities of renin-angiotensin, aldosterone and progesterone are increased leading to water retention and decreased plasma osmolality. ***(Heidemann and McClure, 2003)***

Heartburn during pregnancy is most common and as many as 80% suffer from reflux at term, exacerbated by the supine position. This can be somewhat because of increased intra-abdominal pressure by the gravid uterus and displacement of the gastric axis. ***(Heidemann and McClure, 2003)***

During pregnancy, insulin production rises but is accompanied by increased insulin resistance caused by placental hormones (mainly human placental lactogen). Therefore, any carbohydrate load will cause a greater than normal increase in plasma glucose concentrations. This facilitates placental glucose transfer. The fetus relies on its own production of insulin, because

insulin does not cross the placenta. Poorly controlled maternal diabetes is associated with excessive growth and fetal macrosomia. Maternal hyperglycaemia causes increases in fetal insulin production and after birth this can result in neonatal hypoglycaemia as the carbohydrate load falls immediately. ***(Heidemann and McClure, 2003)***

After the 13th week of pregnancy, about 1.2 extra MJ (300 kcal) per day are required to satisfy the metabolic requirements of a pregnant woman. ***(Artal and O'Tool, 2003)***

There is different evidence on the impact of total carbohydrate intake on insulin sensitivity and in fact, a new dietary intervention found that after 6 months on a low-carbohydrate, high-fat diet, insulin sensitivity increased among obese individuals. However, the source and quality of dietary carbohydrates may differentially optimize insulin action and how to affect the degree of insulin resistance, which is an essential underlying metabolic feature of this syndrome. ***(McKeown et al, 2004)***

Observational studies have observed that fasting insulin concentrations are lower among individuals recording higher dietary fiber or whole-grain intakes after improvement for other lifestyle and dietary factors .The role of high-fiber carbohydrate sources, however, in controlling insulin sensitivity in randomized feeding studies is variable, For standard., some studies report a profitable effect on insulin sensitivity with high consumption of dietary fiber or whole-grain foods, whereas others showed no effect on insulin sensitivity. ***(McKeown et al, 2004)***

The glycemic index, a measure of the glycemic response to carbohydrate- including foods, has been used to physiologically classify dietary carbohydrates. Evidence from observational data recommends that a high dietary glycemic index is correlated with components of the metabolic syndrome, such as increasing triglyceride concentrations and low HDL cholesterol. ***(McKeown et al, 2004)***

Some clinical examinations have demonstrated that low glycemic index carbohydrates promote glycemic control and lipid forms in individuals with and without type 2 diabetes. A measure of both carbohydrate quality and quantity define as the glycemic load, has been associated with increased risk of type 2 diabetes in some observational studies. To date, no observational study has examined the glycemic index and glycemic load of the diet in relation to insulin resistance or the metabolic syndrome. ***(McKeown et al, 2004)***

Dietary recommendations highlight the benefits of high-carbohydrate, low-fat diets in reducing chronic diseases. Still, increasing carbohydrate intake may adversely influence blood lipid and lipoprotein concentrations and glucose metabolism, predisposing some individuals to develop the metabolic syndrome. Whereby, explaining the association of carbohydrate nutrition with metabolic syndrome may produce a strategy for early intervention in the natural progression of type 2 diabetes mellitus. ***(McKeown et al, 2004)***

High levels of dietary fiber intake are associated with a significant reduction in the prevalence of diabetes based on estimates from prospective cohort epidemiological studies. Five epidemiological studies suggested 19% experienced a protective effect from high total dietary fiber intake, while 11 estimates based on over 427,000 individuals with high levels of whole grain or cereal fiber consumption suggested there was a 29% reduction in the development of diabetes.Thus, epidemiological studies suggest that higher levels of dietary fiber intake play a significant protective role with respect to diabetes that is independent of other dietary factors. ***(Anderson and Baired, 2009)***

Recently, the Finnish Diabetes Prevention Study reported a RCT in which individuals with the highest level of fiber consumption had a 62% reduction in progression of prediabetes to diabetes over a 4.1-year period compared to those with the lowest fiber intake. This appears to be the first long-term documentation of the protective effects of fiber consumption with regard to the progression of prediabetes to diabetes. ***(Anderson and Baired, 2009)***

There are many positive effects of physical activity on the mother, such as reduces the risk of excessive weight gain, gestational diabetes, preeclampsia, premature birth, varicose veins, deep vein thrombosis and low back pain. It additionally reduces the duration of labor and complications at childbirth, fatigue, stress, anxiety and depression, leading to an improved sense of wellbeing. ***(Biase et al, 2009)***

However, the potential benefits for the fetus can be summarized as follows: improvement of placental function with increased amniotic fluid, flow and volume of the placenta, fetal vascular function, placental villous tissue and speed growth, neuronal development and reduced percentage of fetal fat. ***(Biase et al, 2009)***

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All women should understand the importance of physical activity and how to safely exercise during pregnancy and in the postpartum period. Providing a woman with an adequate prescription of physical exercise can encourage her to take part in safe and effective activities throughout her pregnancy, in the absence of contraindications. ***(Biase et al, 2009)***

Physical exercise is highly recommended to the broad population before and through pregnancy, and to women suffering from gestational diabetes and to populations at risk for GDM. Aerobic and strength exercise, each of those exercises will verify higher insulin sensitivity, increased glucose uptake, smaller weight gain, delayed begin of hypoglycemic agent medical aid, a reduced quantity of administered insulin, and it conjointly improves cardio-respiratory fitness (Level III B) in women with GDM. ***(Biase et al, 2009)***

However, any kind of physical activity is not perpetually sufficient to ensure proper metabolic control; therefore, it is necessary to use insulin therapy to manage maternal hyperglycemia. One of the intervention studies has shown that regular physical activity during pregnancy can improve other outcomes, such as 58% risk reduction of having an infant with macrosomia and 34% risk reduction of having a preterm delivery. ***(Biase et al, 2009)***

The majority of pregnant women with and without GDM can safely perform aerobic exercises of moderate/vigorous intensity. These include, such as walking, running, dancing, strength machines and weightless body activities, such as cycling, different aquatic activities, exercises on the chair, hand-crank ergometer. The strength work is safe and effective when adapting the insulin (where necessary) and checking the hyperglycemia; weightlifting equipment exercises using progressive resistance elastic bands for arms, legs, abdomen and back. ***(Biase et al, 2009)***

The exercise must sew each mother's physical condition with mild to moderate intensity. The most up-to-date guidelines recommend adding a slight strength activity to routine physical activity. A high risk of falling activities (horse riding, downhill skiing, etc.) or abdominal trauma should be discouraged. ***(Biase et al, 2009)***

Sports with high potential for physical contact (such as ice hockey, football, and basketball) can cause severe trauma to the mother and fetus both and should, therefore, be discouraged. During pregnancy, diving should be avoided because the fetus is at risk of decompression sickness. Caution should be observed in practicing physical exercise at high altitude (>2500 m). (9) ***(Biase et al, 2009)***

High-intensity Interval Training can be explained as 'brief pauses of vigorous activity interspersed with periods of low activity or rest', which produces a strong acute physiological response (Fig. 1). A number of HIIT protocols have been assumed in the literature. The majority of interventions use high-intensity intervals that last between 1 and 4 min. ***(Jelleyman et al, 2015)***

The purpose of HIIT is to accumulate activity at an intensity that the participant would be incapable to sustain for prolonged periods (i.e.80– 95% of peak oxygen consumption (V: O2peak) or >90% of maximum heart rate (HR max), therefore, to allow the subsequent interval to be completed at the wanted intensity the recovery time should be enough and sufficient. The total duration of a HIIT session tends to be ≥20 min, which actually makes it equivalent with recommendations and tips for moderate intensity continuous training (MICT), in terms of duration. ***(Jelleyman et al, 2015)***

Also there is a sub-category of HIIT involving 10–30 second intervals and intensities often exceeding 100% V: O2peak. The wide majority of the published HIIT research, especially in clinical populations, has used exercise modalities including cycling, walking, and running, mostly carried out on stationary cycles and treadmills. However, other equipment and devices, such as cross-trainers/elliptical, are flexible options for some. Evidently, there is a clear variation during the literature and it still remains to be determined whether an optimal HIIT protocol exists for metabolic disease management. ***(Jelleyman et al, 2015)***

A number of molecular adaptations have been identified within skeletal muscle following HIIT (Fig. 1). Skeletal muscle is the main site for glucose disposal via insulin- and noninsulin-mediated glucose uptake; the latter plays a large role in regulating metabolism. Therefore, it stimulated by muscular contraction. ***(Jelleyman et al, 2015)***

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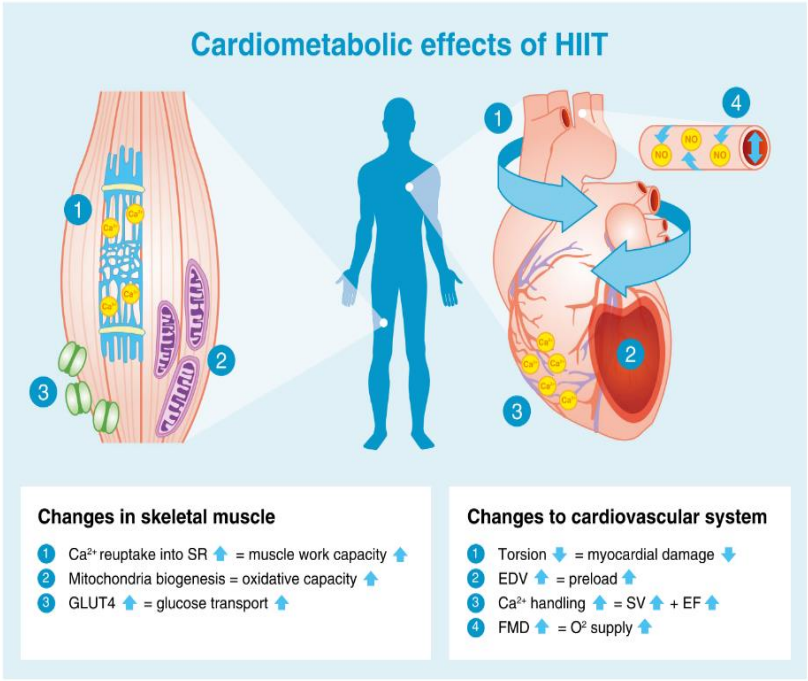

Cardiometabolic effects of HIIT. The figure depicts the previously reported muscular and cardiovascular impact of HIIT in those with common metabolic diseases. In boxes of text: upward arrow, increase; downward arrow, decrease. EDV, end diastolic volume; EF, ejection fraction; FMD, flow mediated dilation; SR, sarcoplasmic reticulum; SV, stroke volume

Fig (2): Cardiometabolic effects of exercise training

They should be retested between 24 and 28 weeks of gestation ***(Setji et al., 2005).***

Homeostasis model assessment (HOMA): is a rapid, simple process for assessing β-cell function and insulin resistance (IR) from basal fasting glucose and insulin or C-peptide concentrations. It has been recorded in >500 papers, 20 times more frequently for the evaluation of IR than β-cell function, is an approved method to measure insulin resistance from fasting glucose and insulin. ***(Wallace et al., 2004*)**.

a measurable test that predicts insulin sensitivity directly by measuring insulinemia and fasting blood glucose and explains the actual bond with the hyperinsulinemic-euglycemic clamp technique described as HOMA, observed as a gold standard in the measurement of insulin sensitivity Therefore, it must be recorded an essential choice for the common complex and challenging techniques in the evaluation of IR in humans. The result for the diagnosis of IR is HOMA-IR higher than 4. ***(Geloneze and Tambascia, 2006).***

HOMA is created to predict the homeostatic concentrations of fasting insulin and glucose, which originate from alternating degrees of β-cell insufficiency and insulin resistance. The pattern is nonlinear but can be directly approximated.

There are two types of HOMA scores are currently being assessed in clinical patients for determining fasting glucose and insulin levels. HOMA IR = insulin resistance = (fasting insulin in mU/L) × (fasting plasma glucose in mmol/L)/22.5. HOMA B = B-cell function [%] = 20 × (fasting insulin in mU/L)/ [(fasting glucose in mmol/L) - 3.5]. We divided the two types of HOMA scores following glucose ingestion at 0, 30, 60, 90, 120, 150, and 180 min ***(Meir et al., 2010***)

Patients have diagnosed as insulin resistant when HOMA ≥4, Fasting insulin was≥12mU/l and fasting plasma glucose ≥ 7 mmol/L (126mg/dl**)** ***(Katsuki et al., 2001)***

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