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Role of Antioxidants and Physical Exercise in the Management of Gestational Diabetes

Khushpreet Kaur[1], Anita Kochhar[2]

Research Scholar, Department of Food and Nutrition, College of Home Science, PAU, Ludhiana

Professor, Department of Food and Nutrition, College of Home Science, PAU, Ludhiana

Abstract: ***The incidence of gestational diabetes mellitus is increasing all over the world and becoming the problem of significant importance. The literature reports indicate that worldwide prevalence of gestational diabetes mellitus has found to range from 0.6 to 13.7%. The prevalence in India varies from 3 to 15 %. Gestational diabetes is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy, especially during their third trimester. Gestational diabetes is caused when the insulin receptors do not function properly. Diet plays a very important role in increasing the blood lipids. Various antioxidants have been developed for oxidative stress treatment in diabetes mellitus, including the use of vitamins and supplements as well as the use of some components of plants and fresh fruits which have demonstrated antioxidant effect in diabetes mellitus patients. Women at high risk for gestational diabetes mellitus may be able to prevent it with lifestyle management during pregnancy. In those who develop gestational diabetes mellitus, dietary improvements and regular physical activity are frequently sufficient to manage hyperglycemia, although insulin and oral medications may be used when these changes are not enough. Management of blood glucose levels ensures better pregnancy outcomes and improves the health of both the mother and the fetus.***

Keywords: Gestational diabetes, Antioxidant, Physical exercise, Management, Pregnancy

1. Introduction

Gestational diabetes is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy, especially during their third trimester. Gestational diabetes is caused when the insulin receptors do not function properly. Gestational diabetes is usually diagnosed during routine screening. It often does not cause any symptoms at all. However, high blood glucose (hyperglycemia) can cause some symptoms, including: Excessive thirst (Polydipsia), excessive appetite (Polyphagia), increased urine production (Polyuria), having a dry mouth, feeling extremely tired, weight loss, impaired vision, poor wound healing.

The incidence of gestational diabetes mellitus is increasing all over the world and becoming the problem of significant importance. Recent data show that gestational diabetes mellitus (GDM) prevalence has increased by 10-100% in several race/ethnicity groups during the past 20 years. A true increase in the prevalence of gestational diabetes mellitus, aside from its adverse consequences for infants in the newborn period, might also reflect or contribute to the current patterns of increasing diabetes and obesity, especially in the offspring. Therefore, the public health aspects of increasing gestational diabetes mellitus need more attention. In India, gestational diabetes mellitus has been found to be more common in women living in urban areas than in women living in rural areas. The trend toward older maternal age the epidemic of obesity and diabetes and the decrease in physical activity and the adoption of modern lifestyles in developing countries may all contribute to an increase in the prevalence of gestational diabetes mellitus. Because gestational diabetes mellitus is associated with several perinatal complications, and because women with gestational diabetes mellitus and their offspring are also at increased risk of developing diabetes later in life, it is critical to assess trends in gestational diabetes mellitus prevalence to allocate appropriate resources to perinatal management and postpartum diabetes prevention strategies (Ferrara 2007).

The literature reports indicate that worldwide prevalence of gestational diabetes mellitus has found to range from 0.6 to 13.7%. The prevalence in India varies from 3 to 15 %. Approximately 650,000 women give birth in England and Wales each year, and 2–5% of pregnancies involve women with diabetes. Approximately 87.5% of pregnancies complicated by diabetes are estimated to be due to gestational diabetes, with 7.5% being due to type 1 diabetes and the remaining 5% being due to type 2 diabetes. The prevalence of type 1 and type 2 diabetes is increasing. The prevalence of gestational diabetes mellitus is increasing worldwide especially in developing countries. In India the prevalence of gestational diabetes mellitus is high and varies according to geographical areas and diagnostic methods employed. According to a random national survey conducted in 2004 the prevalence was 16.55%. In 2008, a hospital based survey showed a combined prevalence of gestational diabetes mellitus and impaired glucose tolerance to be 21.6%. (Sachdev 2011, NICE 2008, Sharmilakrishna *et al* 2011).

The prevalence of diabetes is increasing globally and the total number of people with this condition is projected to rise from 171 million in 2000 to 366 million in 2030. India is no exception, with projected rates of 79.4 million in 2030—a 151% increase from 31.7 million in 2000. The increased prevalence is attributed to the aging population structure, urbanization, the obesity epidemic, and physical inactivity. While all these factors contribute to the epidemic of diabetes, intrauterine exposures are emerging as potential risk factors. The "fetal origin of adult disease" hypothesis proposes that gestational programming may critically influence adult health and disease. The prevalence of gestational diabetes mellitus has markedly been increasing

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in a universally screened urban Chinese female population and has become an important public health problem in China. (Seshiah *et al* 2011, Zhang *et al* 2011).

Gestational diabetes mellitus affects up to 15% of pregnant women worldwide, and in India alone an estimated 4 million women have gestational diabetes mellitus. Women with gestational diabetes mellitus are more likely to give birth to macrosomic or large-for-gestational-age infants. Gestational diabetes mellitus may results in obstructed labour, the death of the mother and the baby and birth injury for the infants. Gestational diabetes mellitus also has long-term health impact, with more than 50% of women with gestational diabetes mellitus going on to develop type 2 diabetes within 5-10 years of delivery. Moreover, infants of women with gestational diabetes mellitus have a higher prevalence of overweight and obesity, and higher risk of developing type 2 diabetes later in life (Leaders 2013)

The prevalence of diabetes mellitus (DM) is increasing worldwide and more in developing countries including India. The increasing prevalence in developing countries is related to increasing urbanization, decreasing levels of physical activity, changes in dietary patterns and increasing prevalence of obesity. As women with gestational diabetes mellitus and their children are at increased risk of developing diabetes mellitus in future, special attention should be paid to this population especially in developing countries (Rajput *et al* 2013).

The prevalence of gestational diabetes mellitus in the United States may be as high as 9.2%, according to a new report from the Centers for Disease Control and Prevention (CDC). According to their study, 1% to 14% of pregnant women in the United States could develop gestational diabetes mellitus annually, depending on the type of diagnostic test used and the population studied. Our results indicate that gestational diabetes mellitus prevalence is as high as 9.2% and is more likely to be reported on the Pregnancy Risk Assessment Monitoring System questionnaire than the birth certificate. (Barbor 2014, Desisto *et al* 2014).

2. Role of Antioxidants

In recent years, antioxidant have gained an utmost importance in preventing some dreaded disease caused by free radicals or oxidants. The free radicals are chemical species, capable of independent existence, possess an unpaired electron on an orbital. These radicals are produced by body's normal use of oxygen and are also generated through environmental pollutants, cigarette smoke, automobile exhaust fumes, radiation, air pollution, pesticides, etc. in traditional scientist nutrition and health care are inter connected and many plants are consumed as food in order to benefit health. Crude extract of fruits, herbs, vegetables, cereals and other plant materials rich in phenolics are increasingly of interest in the food industry because they retard oxidative degradation of lipids and thereby improve the quality and nutritional value of food. In addition to the above compounds found in natural food, vitamin C & E, beta-carotene and alpha tocopherol are known to possess antioxidant potential (Doss and Dhanabalan 2009).

The findings of the study indicate the beneficial effects of antioxidant vitamins E and C both as food and in synthetic form. A combined intake of consumption of vitamins E and C together brought better results in blood lipid levels than consuming vitamin E or C alone. The study has brought out the fact that hyperlipidemics and obese people should consume liberal amounts of fruits and vegetables that are rich in antioxidant vitamins to maintain blood lipid levels. Gestational diabetes induces a condition of oxidative stress leading to an easier membrane lipoperoxidability and consequently easier membrane damage during diabetic gestation. Primary effect of increased oxygen free radical in gestational diabetes is believed to be on enhanced lipid peroxidation. Hydro–peroxides which are major products of lipid peroxidation have been shown to alter prostaglandin biosynthesis which may be responsible for development of diabetes related embryopathy. (Easwaran *et al* 2001, Chaudhari *et al* 2003).

Study suggest that the antioxidant lycopene reduces the development of pre-eclampsia and intrauterine growth retardation in prim gravida women. Nutritious greens of carrot, cauliflower, radish and turnip though available at no cost are always discarded. Various reports have shown that vitamin C is heat labile and is easily destroyed in the process of cooking. Keeping in view, the importance of greens of vegetables for human develop commonly consumed food preparations by incorporating vitamin C rich, cheaply available under exploited greens of carrot, cauliflower, radish and turnip, using different methods (sautéing, deep fat frying, shallow fat frying and pressure cooking) of cooking and to determine the retention of vitamin C in cooked greens. (Sharma *et al* 2003, Kaur and Kochar 2005).

Results of the study brought out the importance of beta carotene and vitamin A, the two important antioxidants in the diets of diabetic patients for reducing the incidence of complications. Vitamin C is an essential antioxidant that is required to protect endothelial cells from oxidative challenge even in the presence of a vast molar excess of glutathione. Vitamin C protects endothelial cells from oxidative stress by neutralizing the effects of oxidative species and decreasing blood cell-endothelial cell interactions, while glutathione modulates the redox properties of vitamin in endothelial cells. Clinical studies have revealed that vitamin C can reverse endothelial dysfunction under different pathological conditions such as hypercholesterolemia, hypertension, smoking, diabetes, and atherosclerosis. (Vasanthamani and Rema 2006, Montecinos *et al* 2007).

Gestational diabetes mellitus induces oxidative stress in the fetus. Furthermore, study there was a significant positive correlation between the levels of serum protein thiol in normal and gestational diabetes mellitus maternal and cord blood samples suggesting that excessive free radical production as seen in gestational diabetes mellitus state could lead to an adaptive response in terms of protein thiol as a sacrificial antioxidant. Moreover, a significant positive correlation that was observed in serum total glutathione-S-transferasc glutathione-S-transferasc level in gestational diabetes mellitus (maternal and cord blood) may be to combat the oxidative stress in such cases (Dey *et al* 2008).

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Antioxidant vitamins, with the ability to stabilize highly reactive free radicals, act as the first line of defense against free radical attack and lipid peroxidation. Vitamins E (α-tocopherol) and C, have differences in the contribution they make to antioxidant potential, as vitamin E is the major lipid soluble chain-breaking antioxidant in cell-membranes while vitamin C is an important aqueous phase antioxidant. Antioxidants may act synergistically, for instance, when vitamin C regenerates α-tocopherol from the tocopherol radical, this 'sacrificial' antioxidant acts more by sparing vitamin E than by recycling. The important role of vitamin C in gestational diabetes, suggests that changes in its concentration may influence susceptibility of vascular endothelium to oxygen toxicity. Thus, study on vitamin C concentration may provide a means of assessing the total capacity of the chain-breaking antioxidants to prevent lipid peroxidation in plasma and it might be important to evaluate the effectiveness of potential antioxidant defense systems in limiting scale. This study, further, provides evidence for the relationship between plasma vitamin C levels during the pregnancy and gestational diabetes (Suhail *et al* 2010).

The group eating the unhealthy "Western" diet with no added antioxidants had significantly higher rates of inflammation and oxidative stress than the other groups, and their offspring were larger and had higher rates of glucose intolerance. The Western diet group that consumed added antioxidants, however, produced offspring with markedly lower rates of glucose intolerance and no obesity (Huff 2011).

Normal human pregnancy is considered a state of enhanced oxidative stress. In pregnancy, it plays important roles in embryo development, implantation, placental development and function, fetal development, and labor. However, pathologic pregnancies, including gestational diabetes mellitus, are associated with a heightened level of oxidative stress, owing to both overproduction of free radicals and/or a defect in the antioxidant defenses. This has important implications on the mother, placental function, and fetal well-being. Increased antioxidant intake can reduce the complications of gestational diabetes mellitus in both mother and fetus. This review provides an overview and updated data on current understanding of the complications associated with oxidative changes in gestational diabetes mellitus (Lappas *et al* 2011).

Oxidative stress occurs in gestational diabetes and antioxidant defense mechanisms are inadequate. Serum levels of advanced oxidation protein products and malonyldialdehyde are higher in gestational diabetes mellitus patients when compared to healthy individuals, and may be useful markers in gestational diabetes mellitus. Various antioxidants have been developed for oxidative stress treatment in diabetes mellitus, including the use of vitamins and supplements as well as the use of some components of plants and fresh fruits which have demonstrated antioxidant effect in diabetes mellitus patients. In some recent studies, some drugs routinely used in the treatment of diabetes mellitus also demonstrated antioxidant effects. (Maitra *et al* 2012, Zatalia and Sanusi 2013).

3. Role of Physical Exercise

Physical activity has long been known for its role in improving glucose homeostasis through its direct or indirect impact on insulin sensitivity via several mechanisms. For instance, physical activity has independent effects on glucose disposal by increasing both insulin-mediated and non–insulin-mediated glucose disposal. Physical activity can also exert long-term effects on improvement in insulin sensitivity through increased fat-free mass. Furthermore, the benefits of preventing or delaying the onset of type 2 diabetes among non-pregnant individuals have been reported repeatedly. Therefore, physical activity may have the potential for preventing GDM and related adverse health outcomes. Along with nutrition therapy and insulin therapy it is also necessary to get regular physical exercise. Regular physical activity helps lower blood sugar by moving the glucose into the cells and also by increasing sensitivity to insulin. Aim for moderately vigorous exercise on most days of the week, but first consult with the doctor (Tobias *et al* 2011, Majumdar 2013).

Exercise training results in sustained insulin sensitivity and improves glucose clearance. Because these functions are altered in gestational diabetes, exercise should be considered not only optional, but preferable, because it obviates insulin therapy. During exercise, plasma concentrations of glucose counter regulatory hormones play an important role in maintaining glucose homeostasis. These hormones include norepinephrine, epinephrine, cortisol, glucagon, and growth hormone. Women who exercised weekly for >30 min at some time during pregnancy had a lower risk of gestational diabetes mellitus, although this result was shown for only morbidly obese women. In addition, data that were nationally representative of women with live births indicated that those who began physical activity during pregnancy had less risk of development of gestational diabetes mellitus than did those who were inactive during pregnancy. In the same study, women with activity levels above the median had a 67% lower risk of gestational diabetes mellitus than those who performed less physical activity. In a recent meta-analysis of 4401 women, which included 361 gestational diabetes mellitus cases, exercise in early pregnancy was related to a 24% decreased risk of gestational diabetes mellitus. (Bung *et al* 1991, Dye *et al* 1997).

Several studies have linked physical activity before and/or during pregnancy to a decreased risk of gestational diabetes mellitus. Compared with those who were inactive, women who participated in any recreational physical activity during the year before pregnancy experienced a 66 percent reduction in risk of gestational diabetes mellitus. Women who engaged in physical activity for <4.2 hours per week were 42 percent less likely to develop gestational diabetes mellitus. During the index pregnancy, 615 women (67.7 percent) reported participating in any recreational physical activity. Compared with inactive women, these women experienced a 31 percent reduction in risk of gestational diabetes mellitus. They reported that women who did not exercise during this time period, compared with active women, experienced a 1.9-fold increase in risk of gestational diabetes mellitus (Dempsey *et al* 2004).

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Authors concluded that the recumbent bicycle and upper body ergometer were the safest forms of aerobic exercise for pregnant women. A potential benefit of exercise in women with gestational diabetes mellitus is improved glycemic control. One small trial randomized women with gestational diabetes mellitus to diet and exercise with an arm ergometer versus diet alone for 6 weeks. Researchers found that the diet-and-exercise group had a significant decrease in glycated hemoglobin levels and in both fasting and 1-hour plasma glucose levels during a glucose challenge test compared to the diet-alone group. Based on the potential benefits of exercise in women with gestational diabetes mellitus, the American Diabetes Association recommends starting or continuing a program of moderate exercise in women without medical or obstetrical contraindications. In addition, certain types of exercise appear to have potential benefits in women without any contraindications (Setji *et al* 2005).

Another study advocates the usefulness of exercise in the treatment of gestational diabetes and suggest that exercise could decrease the risk of gestational diabetes mellitus. Caloric restriction and exercise result in limited weight gain in obese subjects with gestational diabetes mellitus, less macrosomic neonates, and no adverse pregnancy outcomes. (Weissgerber *et al* 2006, Artal *et al* 2007).

Total physical activity before pregnancy or during early pregnancy was significantly associated with a lower risk of gestational diabetes mellitus. Higher levels of physical activity before pregnancy or in early pregnancy are associated with a significantly lower risk of developing gestational diabetes mellitus. Accumulative evidence has suggested that physical activity during pregnancy may be related to gestational diabetes mellitus. By increasing insulin sensitivity and improving glucose tolerance via several mechanisms, physical activity has a beneficial effect on many aspects of insulin resistance syndromes. After an episode of physical activity, insulin sensitivity was improved for up to 48 hours by increasing cellular sensitivity to circulating insulin. In addition to this acute effect, longer-term, even relatively modest, increases in habitual physical activity induce adaptations that can profoundly affect glucose tolerance and potentially decrease gestational diabetes mellitus risk. Long-term improvement in glucose tolerance and increased insulin sensitivity may also result from physical activity induced decreases in fat mass and increases in lean muscle mass. (Tobias 2011, Tobias *et al* 2011, Zhang and Ning 2011).

A supervised program of moderate-intensity exercise performed throughout pregnancy was associated with a reduction in the rate of cesarean, instrumental deliveries and can be recommended for healthy women in pregnancy. Physical activity during pregnancy may prevent both gestational diabetes mellitus and possibly later-onset type 2 diabetes, and engaging in regular physical activity before pregnancy frequently has been associated with a reduced risk of developing gestational diabetes mellitus. In a recent clinical trial, a moderate physical activity program performed thrice weekly during pregnancy was found to improve levels of maternal glucose tolerance in healthy, pregnant women and higher levels of physical activity participation before pregnancy or in early pregnancy significantly lower the risk of developing gestational diabetes mellitus. Women at high risk for gestational diabetes mellitus may be able to prevent it with lifestyle management during pregnancy. In those who develop gestational diabetes mellitus, dietary improvements and regular physical activity are frequently sufficient to manage hyperglycemia, although insulin and oral medications may be used when these changes are not enough. Management of blood glucose levels ensures better pregnancy outcomes and improves the health of both the mother and the fetus. Engaging in 30 min of moderate intensity physical activity on most, if not all, days of the week has been adopted as a recommendation for all pregnant women. (Barakat *et al* 2012, Colberg 2013)

Engaging in regular physical activity before pregnancy frequently has been associated with a reduced risk of developing gestational diabetes mellitus. A prospective cohort study among 21765 women in the Nurses' Health Study II showed that physical activity before pregnancy is associated with a risk reduction in gestational diabetes mellitus, and both intense exercise and moderate activity (*e.g.*, brisk walking) bestow a similar risk reduction. Even engaging in leisure time physical activity in advance of becoming pregnant may reduce glucose intolerance during the pregnancy. Being physically active during pregnancy may prevent both gestational diabetes mellitus and possibly later-onset type 2 diabetes. Women who perform recreational physical activity during the year before becoming pregnant experience a reduced risk, but participating in any physical activity during the first 20 week of pregnancy has been shown to lead to close to a 50 percent risk reduction in gestational diabetes mellitus. Engaging in physical activity both before and during pregnancy likely leads to the greatest reduction in gestational diabetes mellitus risk. Engaging in 30 min of moderate intensity physical activity on most days of the week, reaching a minimal total of 150 min per week, has been adopted as a recommendation for pregnant women without medical or obstetrical complications. Health benefits can be derived from daily sessions lasting 20 to 45 min. Compared with less vigorous activities, engaging in an exercise intensity that is at least 60 percent of heart rate reserve during pregnancy, while gradually increasing physical activity increases energy expenditure, reduces the risk of gestational diabetes mellitus, and the more vigorous the exercise, the less total exercise time is required. Prolonged duration physical activity (*i.e.*, lasting over 60 to 90 min when done continuously) usually is not recommended for pregnant women due to heightened concern over possible hypoglycemia or hyperthermia. (Colberg *et al* 2013)

Majority (64%) of respondents were currently exercising during pregnancy and 51% exercised 2–3 times/week. Among the five questions testing knowledge about prenatal exercise, majority (range 60 to 92%) were aware of recommendations. About half had a BMI ≥30. Knowledge about benefits of exercise during pregnancy did not differ significantly between obese and non-obese. Yoga was tried significantly more among non-obese, 65% believed it is beneficial, and 40% had attempted yoga before pregnancy. In our population, the majority believes that exercise,

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including yoga, is beneficial and they are active. (Babbar and Chauhan 2014).

4. Conclusion

It can be concluded from the research studies that the antioxidants and physical exercise play a great role in the management of gestational diabetes.

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