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SM Journal of Community Medicine

Editorial

Influence of Antioxidant Intake on Gestational Diabetes Mellitus: Evidence from Published Studies

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Article Information

Received date: Dec 05, 2016
Accepted date: Dec 06, 2016
Published date: Dec 07, 2016

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Introduction

Gestational Diabetes Mellitus (GDM), known as glucose intolerance is diagnosed for the first time in pregnancy; usually between 24 and 28 weeks of gestation [1-3]. GDM is a common pregnancy disorder that may result in undesirable maternal and birth outcomes [2]. Women with GDM are at risk of obesity, impaired glucose tolerance and Type-II diabetes years after pregnancy [1]. Infants born to GDM mothers also have increased risks of being obese as well as developing diabetes both in childhood and adult life [2,4]. It has been reported that, gestational diabetes affects 4 to 7 % of all pregnancies although prevalence differ among populations [3,5]. In USA, GDM prevalence estimates were between 4.6% and 9.2% in 2014 [6]. There is lack of understanding on the mechanisms that results in GDM although increased insulin resistance during pregnancy has been named as a contributing factor [3-5,7].

Interventions such as dietary, lifestyle, insulin injections and hypoglycemic agents have been used to manage GDM both in the past and presently [5,8-10]. It has been shown that decrease in antioxidant status as well as antioxidant defense mechanism may contribute to the disease processes [11].

Research indicates that the decrease in antioxidant defense in women with GDM may be attributed to enhanced lipid peroxidation which is responsible for membrane damage. Hydroperoxides which are major products of lipid peroxidation, alters prostaglandin biosynthesis, and may further contribute to the disease process by damaging the antioxidant defense system [11,12]. The impaired antioxidant status indicates lower antioxidant defense due to depletion and utilization during pregnancy. Increasing antioxidant stores during pregnancy remains an important part of pregnancy health.

Vitamin-A is an essential fat-soluble vitamin with physiologic functions during pregnancy [13]. Cross-sectional studies in non-GDM and GDM women have revealed both lower and higher status of Vitamin-A levels [5,13]. The status of tocopherol in similar study designs has not been different [12]. Although some studies have revealed that antioxidant intake during pregnancy reduces the risk of GDM, the relation between antioxidant status and the incidence of GDM remains unclear. There is lack of sufficient information about the relationship between antioxidant vitamins and gestational diabetes. To date, very few case control and randomized controlled trials exist in this area.

Current Evidence - Positive Association between Dietary Antioxidants and GDM

We systematically reviewed and Meta-analyzed six [6] identified studies and the outcome points to a positive association between antioxidant intake and GDM. The number of studies and small sample size of these studies might however mare the level of evidence gathered. The studies also used varying diagnostic criteria for gestational diabetes. One study used the American Diabetes Association (ADA) criteria [5], another utilized the National Diabetes Data Group (NDDG) criteria [10]. Carpenter and Coustan criteria was employed by Lau et al [9] whereas American College of Obstetricians and Gynecology (ACOG) criteria for gestational diabetes diagnosis was utilized by one study [14]. Dietary assessment of antioxidant vitamins were conducted using validated FFQ [9,10,15], dietary records [5] and serum blood biochemical analysis [13,14]. Antioxidant assessed included vitamins A, C, E, carotene, lycopene, tocopherol whereas one study measured Total Serum Antioxidant Capacity (TAC) [5], which is the cumulative synergistic capacity of all antioxidants presents in foods rather their individual antioxidant contents. Studies were conducted in Iran [5,13], India [18], Italy [9], Canada [10] and Northern Ireland [15].

Four studies [9,13-15] reporting the effect of vitamin E on GDM were meta-analyzed to determine the extent of evidence. A significant negative effect of vitamin E intake and risk of GDM was observed(OR; 95% CI 0.59; 0.46-0.73).The pooled effect of two studies[13,15] which estimated the effect of alpha tocopherol on GDM outcome also showed a protective effect of alpha tocopherol on GDM (OR; 95% CI 0.88; 0.61-0.71). The pooled risk of Vitamin-A on GDM from two studies [5,9] also showed a protective effect (OR; 95% CI 0.12; 0.007-0.18).

Scarcity of Evidence from Intervention Studies

The result of this meta-analysis indicates that, higher intakes of Vitamin-A and E were inversely associated with risk of GDM. According to Atilli et al [15], significant depletion in antioxidant capacity is the consequence of GDM. This means that, a lower intake of antioxidant vitamins during pregnancy predisposes the mother to GDM. However, data on antioxidant intakes and gestational diabetes is scarce. This makes it difficult to estimate the actual effect these antioxidants may have on gestational diabetes. According to some studies, there may be no depletion of antioxidant in GDM compared to their control groups [14] whereas other results indicate that, some antioxidants, particularly tocopherol intake may be greater in GDM subjects than controls. In this review, Alpha-tocopherol intake was higher in control subjects than in GDM subjects. This calls for larger clinical trials to estimate the overall effect of tocopherol intake in GDM.

Current evidence is largely from observational studies. Ideally, a Randomized Clinical Trial (RCT) would provide the strongest evidence pertaining to the association between antioxidant vitamins and risk of GDM. Again, number of subjects involved in these studies is not large enough to support a strong conclusion. The heterogeneity in these studies also affects pooled estimates, potentially affecting the association observed. Furthermore, the intra-variability among subjects may predispose the antioxidant assessment with measurement error since dietary Food Frequency Questionnaires (FFQ) may not reflect usual intakes.

Conclusion

Although the small number of observational studies do not allow for a conclusion of clinical relevance, current evidence indicates that efforts to encourage populations to consume diets rich in antioxidants, including Vitamin -E and -A could reduce the risks of gestational diabetes mellitus. This is because increased oxidative stress and reduction in antioxidant defense mechanism due to lower antioxidant status may contribute to disease progression in GDM women. Again, GDM could be a risk factor for the development of antioxidant deficiency and could culminate in a higher risk of morbidity and mortality for both the mother and the child.

This shows the importance of monitoring the levels of these vitamins during pregnancy, especially when the mother has diabetes mellitus. Large controlled trials are needed to further evaluate the potential beneficial role of these antioxidants vitamins in the prevention of impaired glucose metabolism during pregnancy. Even though evidence is scarce, pregnant women must be encouraged to include higher amounts of fruits and vegetables, which are important sources of antioxidants in their diets.

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