

Mini Review

Possible Benefits of A Mediterranean Diet During Pregnancy: Prevention and Treatment of Gestational Diabetes

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Introduction

Gestational Diabetes Mellitus (GDM) is a condition discovered back in 1828 by Heinrich Gottlieb Bennowitz, although it was not until later on in 1957 that it became named as such by ER Carrington et al. [1]. Ever since, it has been recognized as a pathology that occurs during pregnancy where the woman exhibits glucose intolerance with onset or first recognition during pregnancy [2] and which can lead to adverse outcomes in both mother and baby [3].

The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study revealed proof that maternal glycaemic control is essential and not having one could lead to severe outcomes in fetus [4]. Recently it has been observed that the prevalence of GDM is increasing [5,6]. This increase, aside from the fact that obesity and sedentary lifestyle have become more common [7], owes to the fact that diagnostic criteria have changed [3] and as a result of it GDM prevalence has been associated with a 3.5 fold increase in our studied sample of pregnant women in Madrid, Spain [6]. The HAPO study [4] triggered the emergence of new criteria (IADPSG) to diagnose GDM and this has been associated with an increase in its prevalence, from 8% (NDDG criteria) and 10, 6% (Carpenter and Coustan) to 35, 5% [6,8] in our area.

Women with GDM experience increased risk of gestational hypertension and, although generally GDM resolves after giving birth, these women have a 7 fold chance of suffering from type 2 diabetes mellitus (T2DM) in the future as well as hypertension and heart disorders [9-11]. Compared to those with normal glucose tolerance, women with GDM also tend to have pregnancies with

Abstract

Gestational Diabetes Mellitus (GDM) is an important problem of public health worldwide since it compromises both the mother's and fetus's health, not only during pregnancy but also later in life. This has become a greater issue with the introduction of new diagnostic criteria (IADPSG), after which the prevalence has increased greatly in our country. Thus, it should become a major priority to dig deep towards the best method of prevention of this metabolic alteration. Several studies have stated the efficacy of a Mediterranean Diet (MedDiet) in regulating insulin resistance and glycaemia daily excursions as well as its potential effects in the treatment of type 2 diabetes. This report aims to state the reasons for which a MedDiet could offset and treat GDM and its complications, focusing our attention on the use of Extra Virgin Olive Oil (EVOO) and nuts as a tool to ensure adherence to this diet.

Keywords: Gestational diabetes mellitus; Mediterranean diet; Prevention; EVOO; Nuts

more obstetric complications resulting in giving birth to macrosomic or Large-for Gestational Age (LGA) offspring [11,12] this being the main complication in women with GDM and which is responsible for a higher rate of admission to the neonatal intensive care unit [6,13]. Maternal hyperglycemia has other detrimental effects on the fetus that is found to suffer from hypoglycemia caused by fetal hyperinsulinemia, which elevates the chances for obesity and diabetes later on [14,15].

Established risk factors of GDM are advanced age, family history of Diabetes Mellitus (DM), both of which are non-modifiable and, regarding the modifiable risk factors, pregestational body weight, obesity and Gestational Weight Gain (GWG) [16,17] which are also the most strongly related to GDM incidence [18,19]. They also happen to be the factors that mostly determine the baby's weight and predispose them to being either macrosomic or LGA [19]. Unfortunately very little pregnancies are actually planned (less than 8% in our population) which makes it rather complicated to control the pregestational weight therefore it should be a main objective to focus on the control of gestational weight gain and obesity during the actual pregnancy. This aims to target a control of glycaemic levels in the mother, which have been seen to have a direct impact on pregnancy, especially in what relates to less cases of macrosomia [20]. As a matter of fact, intensive treatment of hyperglycemia in pregnancy reduces perinatal adverse outcomes [20,21]. Luckily all of these factors can be modified with an adequate nutritional intervention, and it goes without saying that this is the primary approach that should be assessed when looking to prevent and treat GDM.

Influence of maternal diet on offspring

The nutritional environment to which the fetus is exposed during pregnancy will determine long-term outcomes [22]. Aside from the genetic heritage, the mother's lifestyle while pregnant has a direct impact on the health of the baby, tightly linked to components of the metabolic syndrome [23]. As stated previously, all this can lead to perinatal complications like, for instance, having macrosomic babies. However, it is not only this aspect that should worry us, but also the effect the diet has upon the adipose-tissue distribution [24] and the latter of it in postnatal growth and which is prolonged till childhood [25].

This being said, it becomes obvious the imperativeness of meticulously planning pregnant women's nutrition and beginning a nutritional intervention in this group as soon as possible, in order to achieve an adequate BMI and with the purpose of improving short and long term outcomes in health.

Nutritional intervention

Pregnancy exposes the mother to a diabetogenic state where they find themselves to be more prone to suffer from insulin resistance favored by a rise in human chorionic gonadotropin (HCG) and human placental lactogen (hPL) [26]. Regarding this aspect, it would be essential to follow an adequate diet.

Several studies have been conducted to assess whether or not a nutritional intervention is effective when treating women with GDM as well as reducing its associated complications, all mostly proving that indeed it does contribute to the lowering of adverse outcomes. Moreover, interventions seem to succeed more when counseling and nutritional education is included [21,27]. Additionally, other studies have proven that interventions related to physical activity or dietary counseling control GWG [28], reduces shoulder dystocia and fetal overgrowth risk (LGA and macrosomia) when treating mild gestational diabetes [29]. It also proves to reduce hypertensive disorders and preeclampsia in pregnancy [30].

Prevention of GDM and its adverse outcomes are possible without the need to resort to pharmacological treatment, in the same way metabolic disorders such as metabolic syndrome (MetS) or T2DM in particular can be managed solely with a change in lifestyle and diet [31], not only in its treatment but also in terms of its prevention [32,33]

It is important to take into consideration that it is not only important to do the intervention but actually at what point it should be done. An early intervention is essential given that this contributes to the reduction of both maternal and offspring complications [34-36] and as a matter of fact O'Sullivan and coworkers [37] stated the need for this intervention to be started instantly when the pregnant women turns for medical care.

Most studies focus on an intervention based on a low-glycaemic index diet and physical activity. Despite all the evidence there is supporting how a Mediterranean Diet (MedDiet) positively affects patients with T2DM, to date nobody has contemplated the effect this kind of nutrition will have on pregnant women, prevalence of gestational diabetes and perinatal outcomes.

Mediterranean diet intervention

So, why a MedDiet? It is a diet based in a high consumption of whole grains, vegetables, fruits, legumes, olive oil, fish, dietary fiber and nuts, moderate consumption of dairy products and a low one of red and processed meat [38-40]. This provides a high amount of fiber, unsaturated fats, vitamins and natural antioxidants, and small ones of trans and saturated fats. It is a healthy diet that lacks neither macronutrients nor micronutrients. As a matter of fact given its high quantity of vegetables, fruits and olive oils it is a rich source of carotenoids, vitamin C and E [39]. And it is in this aspect, the fact that it is such a complete diet, that it emerges as a potential protective diet pattern against chronic diseases, such as T2DM [37,41]. These favorable effects don't only come from the consumption of fruits and vegetables, or even dietary fiber, its most important feature is the high fat content (unsaturated) of the MedDiet. It enables gastric emptying to be delayed, having an effect on postprandial metabolism, proving to reduce postprandial glucose and enhance insulin levels, all together lowering the glycaemic response [38,42]. Furthermore, it's considered to be a key foundation/pillar in weight-loss strategies [43], with significant difference in comparison to other typically low-fat diets. This is what has raised the interest of investigators in its use in the prevention and treatment of T2DM.

MedDiet in T2DM

GDM is similar to T2DM given that in both cases there is a physiological mishandling of glycaemia levels caused by the insulin resistance to which the individual is exposed. In both groups the main approach is to avoid increases of glucose levels. Concerning GDM, it is rather interesting to comprehend and analyze how T2DM patients are treated, what kind of lifestyle they are lured into and why.

In the management of T2DM, the MedDiet has been suggested and subsequently proved to be an ideal therapy to patients suffering from this condition as a long-term exposition to this diet has shown a reduction in both insulin and postprandial glucose levels [44-46]. Recently, it has also shown effectiveness in its prevention. As a matter of fact, the adherence to a typical MedDiet pattern was associated with a 50% reduction in the risk of T2DM [47].

Given that the key approach to treating T2DM patients is the control of the glycaemic load, which is going to depend on the glycaemic index as well as the proportion of carbohydrates in a meal or food, all of these patients nutrition therapy is primarily focused in the carbohydrate content of the diet and the way it affects postprandial glycaemia. However, latest investigations have determined that in these subjects the importance of the glycaemic load is equal to that of the fat content of the diet, specifically the types of fats: monounsaturated (MUFA) and polyunsaturated (PUFA) [48-55].

Fats and glycaemic control: The quality of fats have been an object of study by many, where unsaturated fats (MUFA and PUFA) have shown to have a desirable effect on insulin resistance, glycaemic control and has been in fact associated with a regression in DM [56]. Therefore despite the fact that fats are energy-dense nutrients, their inclusion in a diet are essential especially regarding their effect on metabolic control. In healthy subjects, MUFA are the ones that are mostly related to a positive response in insulin secretion [48,49]. However, the consumption of both MUFA and PUFA is important

in the management of patients with DM, as well as their ratios to saturated fatty acids (SFAs), being able to control glycaemic levels and ameliorate diabetic complications [50].

Olive Oil: It is the main source of MUFAs in this diet [39]. Consumption of olive oil, a rich source of MUFA, demonstrated to improve insulin response [51] and sensitivity [52]. It also exhibited beneficial effects in terms of impaired glucose intolerance [53], as well as inducing postprandial increment-responses [54, 55]. Moreover, the incorporation of this product is more beneficial when its virgin variety (EVOO) is consumed because it is richer in polyphenol content [57], which favors a lower risk of T2DM because of its anti-inflammatory properties.

Nuts: Aside from EVOO, there are other sources from which we can benefit from these effects in terms of glycaemic control: nuts. These are also high in fats, but mostly a mixture of unsaturated fats such as MUFAs and PUFAs [58]. Like olive oil, nuts have also been related to promoting an adequate glycaemic control, where intervention and observational studies regarding nut consumption have shown benefits on glucose metabolism [59], a decrease in hyperglycemia [59,60] and insulin resistance [61] and control of body weight gain [62,63]. This effect has also been observed when meals are enriched with nuts resulting in a reduction of its acute postprandial glycaemic impact [63].

Almonds have proven beneficial in optimizing postprandial insulin responses [64], not only as snacks but incorporating them in mealtimes, especially before starchy meals, as this significantly reduces postprandial glycaemia [65,66]. Studies have shown that even when consuming high-glycaemic index meals, if nuts such as pistachios, peanuts or almonds are added, the postprandial glucose response is ameliorated by a 30-50% probably because digestion is slowed down [65]. Additionally, the chronic consumption of almonds, 5 times a week during a period of 12-weeks also significantly reduced HbA1c [66]. This provides further proof of to what extent the incorporation of nuts can determine a convenient glycaemic regulation.

Walnuts are also related to diabetes prevention and a significantly lower risk of T2DM [66-67]. They appear to exert a favorable influence in insulin resistance [67-68]. Walnuts differ from other nuts because of their richness in PUFAs content, which is uniquely high in comparison to other nuts [58]. This motivates an elevation of circulating concentrations of PUFAs, hence improving insulin resistance [69].

Along with almonds and walnuts, pistachios have also shown to improve these physiological effects on glucose response [70,71]. In fact, it is emerging as a nutritional strategy for T2DM prevention beyond the use of almonds and walnuts, despite the fact that these last ones contain a higher proportion of PUFAs [58]. The consumption of pistachios can improve glucose and insulin metabolism, alleviating postprandial glucose levels. This effect is seen mostly when they are consumed with carbohydrates [71]. Their beneficial effect is such that incorporating them chronically to our diet can even reverse risks associated with pre-diabetes [72], lower fasting glucose [72,73] and enhance insulin resistance [72]. Furthermore, a regular consumption of pistachio nuts in subjects with MetS have shown to significantly reduce glycaemia 2 hours after 75g glucose challenge [74] playing an important role in the improving risk factors of MetS.

In order to prevent and treat this condition incorporating these types of fats to a diet is as important as for what foods they are substituting. There is evidence that suggests that consuming MUFA and PUFA in substitution to saturated and trans fats [53,69] or carbohydrate foods [75] has beneficial effects on insulin sensitivity and is likely to reduce risk of T2DM.

Oily fish: No doubt oily fish is one of the main food groups, along with others such as whole grains, EVOO or nuts, that confer MedDiet its outstanding reputation. Its importance is also highlighted, and the reason behind it is its high content of unsaturated fats [38]. Indeed, oily fish is a rich source of omega-3 fatty acids, which, like EVOO and nuts, have also proved to have a marked effect on insulin resistance, glycaemia levels, and others metabolic markers [76]. These types of fats help reduce MetS prevalence [77]. Not only do they help manage weight and obesity [78], but they also have favorable effects in terms of glucose homeostasis [79] and glucose tolerance [80]. Moreover, pregnant women with GDM benefited greatly from incorporating oily fish to their diet as the omega-3 fatty acids managed to have favorable effects on insulin metabolism, specifically on insulin resistance [81].

Ongoing study

Will all of this evidence and information stating how a MedDiet rich in unsaturated fats is linked to a risk reduction and successful treatment of T2DM, we cannot help but hope it can also work for GDM. This leads to the proposal of the MedDiet as a possible prevention therapy of this condition.

A recent meta-analysis was performed to determine whether or not a nutritional approach to preventing GDM is effective and concluded it was not [82]. However, the fact that to date none of the previous interventions used the MedDiet as a possible solution should not be overlooked.

Another meta-analysis about the possible lifestyle interventions during early pregnancy, between the 8-10 and 24-28 weeks of gestation [83,84], suggests that all interventions done between these periods of time are effective in terms of GDM prevention. A study conducted by Ruiz-Gracia et al [85] not only identified a low-risk nutritional pattern associated to the prevention of GDM, but also proved how there's an association between lifestyle change during early pregnancy and prevention of GDM. This nutritional pattern was identified as a weekly consumption of >3 nuts, < 4 juices, cookies and pastries and ≤ 1 refined cereals. These results are in concordance with those obtained in other studies where decreasing sugary or sweetened drinks [86,87] alongside with other aspects like increasing physical activity or decreasing the consumption of red and processed meat are also associated to a lower GDM risk. Hence, doing the opposite can be identified as risk factors for developing GDM.

In addition, and in agreement with other studies proving the beneficial effect of MedDiet in T2DM [37,38,41,42,44-46], these results can also be extrapolated to women in their post gestational period, whom also benefited from the adherence to MedDiet as it prevented glucose homeostasis impairment [88].

For this reason, we propose that a lifestyle intervention based on MedDiet and physical activity, starting on the first gestational visits (8-12 weeks) and being maintained during the whole of the pregnancy, in women with normal fasting glucose levels (92 mg/dl),

can reduce the incidence of GDM between the 24-28 weeks, as well as reducing the morbidity in mother, gestation and newborns.

In order to facilitate the access to this kind of diet, the intervention group will be provided with EVOO and pistachio nuts of the Mediterranean region of Spain, which will both help mimic a typical Spanish diet and also serve as a tool to ensure maximum adherence to the MedDiet intervention.

We should hope that all the evidence examined in this report, combined with the fact that generally pregnant women are receptive to interventions that might improve the health of their offspring, might be enough to prove our hypothesis right.

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