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The Relationship Between Gestational Diabetes and Stress: A Literature Review

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Abstract

The incidence of gestational diabetes has been increasing over the past ten to twenty years. The purpose of this literature review is to gather existing literature to examine the relationship between gestational diabetes and oxidative stress. Twenty peer-reviewed articles from two databases were selected to be examined in this review. From these studies, it was found that oxidative stress was higher in women who were diagnosed with gestational diabetes, and supplementation with vitamins and minerals was beneficial in decreasing stress in these women. While these studies can help healthcare providers in educating women who have been diagnosed, more research should be done to reduce gaps in the literature, such as which supplement or group of supplements is most beneficial in decreasing oxidative stress in gestational diabetes.

Introduction

Gestational diabetes is a type of diabetes mellitus that is diagnosed during pregnancy. Insulin needs change throughout pregnancy and the hormones secreted by the placenta can cause an increase in insulin resistance (Murray et al., 2019). While most women can compensate for this through increasing pancreatic insulin production, this does not always occur and leads to episodes of hyperglycemia. This elevation in blood glucose levels leads women to be diagnosed with gestational diabetes, which occurs in 2 to 10% of pregnancies in the United States every year (Centers for Disease Control and Prevention, 2019). This literature review is going to examine the relationship between gestational diabetes and oxidative stress. Oxidative stress occurs in the presence of excessive free radicals in the body, which in turn leads to cellular damage, increased risk for diseases, or exacerbation of existing conditions (Dix, 2018).

Risk factors for gestational diabetes include having a BMI greater than 25, maternal age over 25, having a previous pregnancy with gestational diabetes, a history of abnormal glucose tolerance, a family history of diabetes, having a personal history of pre-diabetes, and ethnicity (Murray et al., 2019). Gestational diabetes is diagnosed between 24 and 28 weeks of gestation by using an oral glucose tolerance test (Murray et al., 2019). Women have baseline fasting blood glucose levels drawn, and then ingest a solution containing 100 grams of glucose. Blood is then redrawn every hour after ingesting the solution for up to three hours (Murray et al., 2019). A diagnosis of gestational diabetes is made if two or more of the blood values are above the threshold (Murray et al., 2019). The threshold for a fasting blood glucose is 95 mg/dL, the threshold rises to 180 mg/dL at one hour, 155 mg/dL at two hours, and 140 mg/dL at three hours after ingesting the glucose solution (Murray et al., 2019).

Gestational diabetes has the potential to adversely affect both mother and baby, leading to conditions such as hypocalcemia, hyperbilirubinemia, and respiratory distress syndrome in the fetus (Murray et al., 2019). The episodes of hyperglycemia can also cause the fetus to be large for gestational age, which increases the risk for injury to the mother during birth (Murray et al., 2019). It is beneficial for nurses to have a clear understanding of gestational diabetes to promote the best outcomes for their patients, as nurses provide education about management of the disease process. Pregnancy can already bring about a myriad of emotions when trying to prepare to care for another human life, thus the diagnosis of gestational diabetes can bring about more anxiety and stress for the mother.

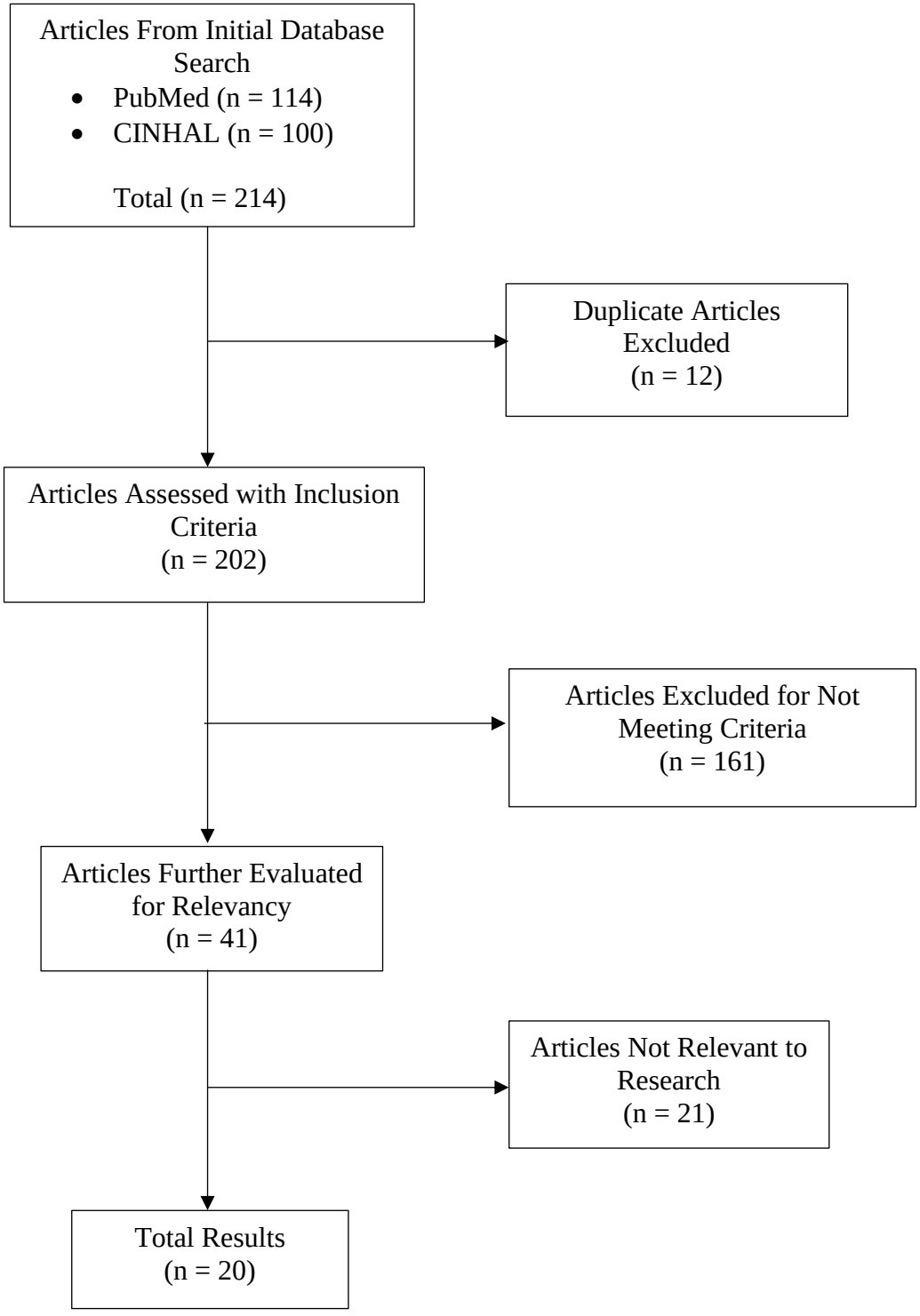
The purpose of this literature review is to further understand the correlation between gestational diabetes and oxidative stress. While many studies have been completed regarding diabetes in pregnancy, some look at all types of diabetes, and others only focus on preexisting diabetes. Many of the studies found while researching for this review focus on the management of oxidative stress after the diagnosis of gestational diabetes instead of prevention. Therefore, more research should be done regarding the prevention of stress, with a focus on gestational diabetes rather than all types to gain a better understanding of the relationship between gestational diabetes and stress.

Methods

For this literature review, the research databases PubMed and CINAHL were utilized. The search terms used in each database were ‘gestational diabetes’, ‘gdm’, ‘gestational diabetes mellitus’, ‘diabetes in pregnancy’, and ‘stress’. To be included in the literature review, the articles needed to be published in the English language, a primary source, peer-reviewed, published within the past 5 years (2016 to 2021), and focused on gestational diabetes. Articles

that did not meet all inclusion criteria were excluded, which yielded a total of 214 articles from both databases. These articles were evaluated for duplication, and 12 were found to have appeared in both databases. Articles were then evaluated on the inclusion criteria through the titles and abstract, resulting in 161 articles being excluded. The remaining 41 articles were further evaluated, which resulted in 20 articles being chosen for this literature review. The selection process is illustrated in Figure 1 below.

Figure 1


Articles From Initial Database Search
PubMed (n = 114)
CINHAL (n = 100)
Total (n = 214)
Duplicate Articles Excluded (n = 12)
Articles Assessed with Inclusion Criteria (n = 202)
Articles Excluded for Not Meeting Criteria (n = 161)
Articles Further Evaluated for Relevancy (n = 41)
Articles Not Relevant to Research (n = 21)
Total Results (n = 20)

Results

In one article, researchers completed a double-blind, randomized study to look at the effects of omega-3 fatty acids and vitamin E on oxidative stress and inflammation in those diagnosed with gestational diabetes (Jamilian, Hashemi, et al., 2017). Participants were split into two groups. One group took a supplement with 100 mg of omega-3 fatty acid and 400 IU of vitamin E, while the other group took a placebo. Fasting blood samples for specific biomarkers of oxidative stress were taken such as nitric oxide, malondialdehyde (MDA), total antioxidant capacity, total glutathione, and high sensitivity C-reactive protein (hs-CRP) (Jamilian, Hashemi, et al., 2017). The researchers found that the supplement had a positive impact on all of these levels except for glutathione and C-reactive protein and therefore concluded that this supplement was beneficial for the use of oxidative stress in gestational diabetes (Jamilian, Hashemi, et al., 2017).

A similar study was done but measured the effects of probiotic supplementation on inflammation and oxidative stress in women with gestational diabetes, completing a double-blind study in which participants were separated into an intervention and a placebo group (Badhnoosh, 2017). Blood samples were taken from the participants to evaluate their nitric oxide, malondialdehyde, total antioxidant capacity, total glutathione, and high sensitivity C-reactive protein levels (Badhnoosh, 2017). The researchers found that the probiotic supplement had a positive influence on total antioxidant capacity, malondialdehyde, and serum C-reactive protein, but not nitric oxide or glutathione (Badhnoosh, 2017). Another study looking at probiotic supplements on the effects of oxidative stress in gestational diabetes found similar results. Researchers found that the supplement used showed a significant decrease in C-reactive protein and tumor necrosis factor (Hajifaraji, 2018).

The effects of antioxidant use in relation to gestational diabetes has also been studied (Maged, 2016). Researchers completed a randomized study in which the intervention group received an antioxidant, 1 gram of ascorbic acid, and the control group received a placebo. All participants self-monitored glucose levels and had blood drawn at the beginning and end of the study to determine the effect of the antioxidant on oxidative markers such as malondialdehyde and glutathione (Maged, 2016). They found the antioxidant supplement helped to increase glycemic control in gestational diabetes and therefore, lowering the need for insulin therapy during the pregnancy (Maged, 2016). The supplement also decreased the level of glutathione significantly when compared to the placebo (Maged, 2016).

The impact of antioxidant status on the risk of gestational diabetes has also been studied (Parast & Paknahad, 2017). Researchers completed a case-control study in which women completed a questionnaire regarding the types of food eaten and the frequency of meals throughout pregnancy (Parast & Paknahad, 2017). Overall, those who were diagnosed with gestational diabetes had less intake of vitamin E, selenium, and zinc compared to those without gestational diabetes (Parast & Paknahad, 2017). This led to the conclusion that eating an antioxidant-rich diet can be protective against the development of gestational diabetes due to less oxidative stress (Parast & Paknahad, 2017).

Another article discussed a different supplement in relation to gestational diabetes. Researchers completed a randomized control study to evaluate the effects of vitamin D and calcium supplementation on oxidative stress in gestational diabetes (Gunasegaran et al., 2020). One group received 1000 IU of vitamin D and 1000 mg of calcium, while the other group received 250 IU of vitamin D and 500 mg of calcium (Gunasegaran et al., 2020). Blood samples were taken before and after the 6-week round of supplementation, comparing the levels of

fasting glucose, lipid levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL), glutathione, serum vitamin D, and serum insulin between the two groups of participants (Gunasegaran et al., 2020). It was noted that the higher supplementation level led to a reduction in fasting blood glucose, LDL, HDL, and had a positive impact on glutathione, thus researchers concluded that the supplements helped to reduce oxidative stress in women with gestational diabetes (Gunasegaran et al., 2020).

A similar study was done but looked at the effects of vitamin D and omega-3 on oxidative stress instead. This study also found a reduction in the markers of oxidative stress when using supplementation (Razavi et al., 2017). Another similar study looked at vitamin D and probiotic supplementation on oxidative stress in gestational diabetes. A double-blind, randomized study was completed, and participants were divided into three groups (Jamilian, Amirani, et al., 2019). One group received both vitamin D and a probiotic, one received only a probiotic, and one received a placebo. Blood samples were taken for comparison, and it was found that the group who received both supplements had reduced fasting plasma glucose, triglyceride levels, malondialdehyde, and C-reactive protein (Jamilian, Amirani, et al., 2019). Researchers concluded that the combination of supplements was the most beneficial in treating oxidative stress.

Another article discussed how a supplement containing magnesium, zinc, calcium, and vitamin D affects oxidative stress in gestational diabetes (Jamilian, Mirhosseini, et al., 2019). Researchers placed participants into two groups, with the intervention group receiving a combination supplement of 100 mg of magnesium, 4 mg of zinc, 400 mg of calcium, and 200 IU of vitamin D (Jamilian, Mirhosseini, et al., 2019). Blood samples were drawn before and after taking the supplement for 6 weeks, evaluating fasting blood glucose, total plasma nitrate, C-

reactive protein, malondialdehyde, and total antioxidant levels (Jamilian, Mirohosseini, et al., 2019). Study results showed the supplement was helpful in reducing oxidative stress because there was a decrease in C-reactive protein, total nitrate, and malondialdehyde levels in those who took the supplement (Jamilian, Mirohosseini, et al., 2019). A similar study evaluated vitamins and antioxidant status in gestational diabetes. The study also included the relationship between progesterone and pancreatic beta cells, which are the cells that release insulin in response to rising plasma glucose levels (Hoffman & Sullivan, 2020). Researchers took samples of cells and treated them with a solution containing progesterone peroxidase-conjugated antibodies, evaluating the protective effect of vitamin E and C on preventing progesterone-induced apoptosis (Borçari et al., 2020). It was determined that vitamin E and C are beneficial in reducing oxidative stress, as there was a protective effect on the cells treated with the vitamins beforehand, which could be beneficial in the treatment of gestational diabetes (Borçari et al., 2020).

The effects of selenium supplementation on oxidative stress in women with gestational diabetes has also been studied (Saifi et al., 2019). Participants were divided into two groups in which one received a placebo and the other took 50 mg of selenium per day. Researchers analyzed fasting blood glucose and antioxidant markers such as malondialdehyde (Saifi et al., 2019). Selenium supplementation was shown to significantly decrease fasting blood glucose and allowed for better glycemic control, but there was not a significant difference in antioxidant levels (Saifi et al., 2019).

Research has also evaluated the placental expression of nuclear factor erythroid 2 (Nrf2) and antioxidant enzymes in relation to gestational diabetes (Manoharan et al., 2019). The study aimed to identify the presence of protective factors for oxidative stress in the placenta when the mother is diagnosed with gestational diabetes. Researchers completed a cross-sectional study,

using blood and placental samples from women and found that malondialdehyde levels and Nrf2 were elevated in those with gestational diabetes (Manoharan et al., 2019). The blood level of Nrf2 was similar in women with and without gestational diabetes but was increased in the placenta for those with gestational diabetes (Manoharan et al., 2019). This led the researchers to conclude that Nrf2 is a potential protective factor that prevents the fetus and placenta from undergoing excessive oxidative stress when diagnosed with gestational diabetes (Manoharan et al., 2019).

A similar study hypothesized that lipoprotein phospholipase could potentially be a protective factor against oxidative stress and gestational diabetes (Schliefsteiner et al., 2017). Researchers took samples of placenta and fetal cord blood to assess lipoprotein-associated phospholipase (Schliefsteiner et al., 2017). These levels were also compared with LDL and HDL, which showed that phospholipase levels were increased in all pregnancies with gestational diabetes but to a different degree depending on the lipoprotein carrier (Schliefsteiner et al., 2017). They found that when LDL was the carrier, there was increased inflammatory activity, but inflammation decreased when HDL was the carrier (Schliefsteiner et al., 2017). Increased inflammation led to more oxidative stress; therefore, more research should be completed, focusing on methods to decrease negative phospholipase (Schliefsteiner et al., 2017).

Rueangdetnarong et al. (2018) compared oxidative stress biomarkers in those with gestational diabetes to those without. Researchers completed a prospective study, measuring the level of 8-isoprostane, tumor necrosis factor, and interleukin 10, with a follow up at birth to obtain fetal cord blood (Rueangdetnarong et al., 2018). It was determined that glycemic control does not directly affect oxidative stress, despite elevated levels of tumor necrosis factor and isoprostane in gestational diabetes (Rueangdetnarong et al., 2018). Researchers concluded that

both glycemic control and reduction of oxidative stress would be beneficial in preventing adverse pregnancy outcomes related to gestational diabetes (Rueangdetnarong et al., 2018).

Li et al. (2016) completed a prospective case-control study, comparing the plasma markers of oxidative stress in women with gestational diabetes between the second and third trimesters. Blood samples were taken to evaluate fasting blood glucose, triglyceride levels, and oxidative stress levels such as 8-isoprostane (Li, Yin, et al., 2016). As gestation progressed, the levels of oxidative stress increased, but further research should be done to determine the predictive nature of oxidative stress of the development of gestational diabetes and the outcomes (Li, Yin, et al., 2016).

An observational study evaluated the relationship between oxidative stress and inflammatory cytokines on gestational diabetes (Sudharshana et al., 2018). Researchers evaluated levels of tumor necrosis factor, interleukin-6 and 8, glutathione, superoxidase dismutase, and uric acid (Sudharshana et al., 2018). They took blood at the time women were diagnosed with gestational diabetes and followed up with them after giving birth. Researchers found that uric acid and tumor necrosis factor were elevated in women with gestational diabetes, and they also had decreased levels of glutathione and superoxidase dismutase (Sudharshana et al., 2018). The study also found that those with gestational diabetes were at an increased risk for preeclampsia (Sudharshana et al., 2018).

Li et al. (2019) studied how advanced glycation end productions (AGEs) and adipocytokines influenced oxidative stress in placental tissue in women with gestational diabetes. Researchers obtained placental samples after women gave birth to test levels of malondialdehyde, AGEs, and adipocytokines (Li, Dong, et al., 2019). They found those with gestational diabetes had higher levels of malondialdehyde and higher levels of AGEs and

adipocytokines, leading to the conclusion that increased AGEs and cytokines are related to increased oxidative stress in gestational diabetes (Li, Dong, et al., 2019).

Another study looked at how gestational diabetes influenced oxidative stress and beta amniolevulinate dehydratase (Rodrigues et al., 2017). Researchers took blood samples from women in their third trimester with and without gestational diabetes, comparing oxidative stress markers such as malondialdehyde and amniolevulinate (Rodrigues et al., 2017). It was found that oxidative stress markers were increased, and there was a similar decrease in amniolevulinate for those with gestational diabetes (Rodrigues et al., 2017). Researchers concluded that amniolevulinate is sensitive to hyperglycemia and could potentially increase oxidative stress on the body; therefore, further research should be done to gain a better understanding of the effect of low amniolevulinate during pregnancy (Rodrigues et al., 2017).

The impact of diet on oxidative stress in patients with gestational diabetes has also been studied using a randomized control trial to determine the effect of a low glycemic index diet versus a standard diet. LDL and conjugated dienes (CD) were compared in both population groups (Seider et al., 2018). Though a standard diet can decrease CD and LDL levels, a low glycemic index diet decreased these levels more significantly and can be beneficial in reducing oxidative stress in women with gestational diabetes (Seider et al., 2018). Another group of researchers completed a case-control study to determine how dietary total antioxidant capacity affected gestational diabetes (Daneshzad et al., 2020). They assessed dietary total antioxidant capacity by looking at the ferric reducing ability of plasma (FRAP), total radical-trapping antioxidant parameter (TRAP), and Trolox equivalent antioxidant capacity (TEAC) (Daneshzad et al., 2020). Participants completed a diet recall survey and gave blood samples. When comparing those with gestational diabetes to those without, the researchers found that FRAP and

vitamin C levels were lower in those who had gestational diabetes (Daneshzad et al., 2020). Researchers concluded that those with higher FRAP were at less of a risk for developing gestational diabetes and that having a diet high in antioxidants can reduce blood glucose levels (Daneshzad et al., 2020).

Table 1

Author	Year	Sample Size	Purpose of the Study	Intervention Tested	Key Findings
Badehnoosh et al.	2017	60 women	Evaluate the effects of using probiotic supplements on biomarkers of oxidative stress in women with gestational diabetes	30 women received a daily probiotic capsule for 6 weeks and 30 women received a placebo	• Those taking the supplement had a statistically significant reduction in hs-CRP, MDA, and fasting glucose levels • They also had increased total antioxidant capacity • There was not a significant difference in insulin needs
Borcari et al.	2020	Cells from the American Type Culture Collection were used	Study the effects of progesterone on biomarkers of oxidative stress	RINm5F and MDA-MB-231 cells were incubated on plated with progesterone levels that would match what a	• Cells treated with progesterone alone showed a loss of membrane integrity and a higher

				woman would secrete during pregnancy, some plates were treated with a vitamin E or vitamin C solution prior to introducing the progesterone	occurrence of apoptosis • Vitamins E and C helped to decrease progesterone-induced apoptosis and could be useful in the prevention and treatment of gestational diabetes
Daneshzad et al.	2020	463 women	Determine the association between dietary levels of antioxidants and gestational diabetes	200 women who were diagnosed with gestational diabetes and 263 who were not completed dietary record forms for 24 hour periods to determine the ferric reducing ability of plasma (FRAP), total radical antioxidant parameter (TRAP), and Trolox equivalent antioxidant capacity (TEAC)	• Total energy, protein, and selenium were elevated in those with gestational diabetes when compared to control, while FRAP was lower. This showed that antioxidants were helpful in the maintenance of glucose homeostasis • There was no significant difference for TRAP and TEAC
Gunasegaran et al.	2020	70 women	Determine how vitamin	34 women received	• Those who received

			D and calcium supplements effects biomarkers of oxidative stress in gestational diabetes	1000 IU of vitamin D and 1000 mg of calcium daily for 6 weeks and 36 women received 250 IU of vitamin D and 500 mg of calcium	higher supplementation had lower fasting glucose level and total cholesterol levels • Both groups showed an increase in glutathione levels
Hajifaraji et al.	2018	64 women	Measure the effect of a probiotic supplement on oxidative stress biomarkers in women with gestational diabetes	32 women received a probiotic supplement containing 4 bacterial strains once a day for eight weeks and 32 women received a placebo	• Blood glucose levels showed no statistical difference between the groups • Hs-CRP and TNF-α were significantly lower in the probiotic group compared to the control
Jamilian, Amirani, et al.	2019	87 women	Determine how vitamin D and probiotic supplements effect oxidative stress and pregnancy outcomes in women diagnosed with gestational diabetes	30 women received 50,000 IU of vitamin D every 2 weeks and a daily probiotic, 29 women received the probiotic only, and 28 women received a	• Co-supplementation significantly reduced fasting plasma glucose levels, hs-CRP, MDA, and triglyceride levels compared to the placebo

				placebo for 6 weeks	• Those taking both supplements also showed an increase in total HDL levels and improved glycemic control
Jamilian, Hashemi, et al.	2017	60 women	Determine the effects of using omega-3 and vitamin E supplements on the biomarkers of oxidative stress in women with gestational diabetes	30 women received daily supplements of omega-3 and vitamin E and 30 women received a placebo	• Those receiving the supplements high significant increases in plasma TAC and decrease in plasma MDA • Those receiving the supplement also showed a decrease in rates of hyperbilirubinemia in newborns
Jamilian, Mirhosseini, et al.	2019	60 women	Determine how to use of magnesium, zinc, calcium, and vitamin D supplements effect inflammation and oxidative and stress as well as pregnancy outcomes in women diagnosed with	30 women received 100 mg magnesium, 4 mg zinc, 400 mg calcium, and 200 IU of vitamin D daily while 30 women received a placebo	• The co-supplementation resulted in a significant decrease in FPG, serum hs-CRP, and plasma MDA compared to placebo

			gestational diabetes		
Li, Dong, et al.	2019	152 women	Determine how advanced glycogen end products (AGEs) effect oxidative stress in women with gestational diabetes	72 women who were diagnosed with gestational diabetes and 80 women not diagnosed were part of a control group, tissue samples were taken at delivery from the placenta	• Levels of AGEs and interleukin 6 were significantly elevated in those with gestational diabetes • The level of MDA was significantly increased when compared with the control, which leads to the positive correlation between elevated AGEs and oxidative biomarkers
Li, Yin, et al.	2016	52 women	Determine how biomarkers of oxidative stress compare in the second and third trimester for women with gestational diabetes with healthy women	22 women with gestational diabetes and 30 healthy women gave blood samples after a 12 hour fast at 16-20 weeks, 24-48 weeks, and 32-36 weeks to test levels of 8Isop and GPX-3	• Levels of GPX-3 and 8Isop were significantly increased at 16-20 weeks as well as 32-36 weeks in women with gestational diabetes which shows that oxidative damage is higher in patients with

					gestational diabetes
Maged et al.	2016	200 women	Determine the effect of using ascorbic acid in women on oxidative markers in women with gestational diabetes and relation to fetal outcome	100 women received 1 gram of ascorbic acid daily and 100 women received a placebo	• Antioxidant use decreased the dose needed to control blood sugar • Neonatal birth weight was lower for those receiving the antioxidant • Plasma glutathione increased by 43% in the antioxidant group compared to the control group
Manoharan et al.	2019	80 primigravid women	Determine the relationship between the expression of placenta nuclear factor erythroid 2-related factor 2 (Nrf2) and the levels of antioxidants and compare them in women who are diagnosed with gestational diabetes and those who do not	40 women diagnosed with gestational diabetes and 40 women without complications were selected and blood samples were collected in the third trimester at 32 weeks and 4 days as well as umbilical blood at delivery to be compared	• MDA levels and the MDA/TAS ratio in maternal plasma and cord plasma were elevated in women with gestational diabetes • There was an increase in Nrf2 in women with gestational diabetes in correlation with an increase in

					oxidative stress • Authors hypothesize that Nrf2 was play a role in protecting the placenta from elevated oxidative stress
Parast & Paknahad	2017	80 women	Compare antioxidant capacity and antioxidant nutrient intake in women with and without gestational diabetes	40 women with gestational diabetes and 40 women without filled out a food frequency questionnaire to determine the intake of antioxidants	• Vitamin E, zinc, and selenium intake was significantly lower in women diagnosed with gestational diabetes which are antioxidants found in food • Dietary antioxidants could be a protective factor and help to manage gestational diabetes
Razavi et al.	2017	120 women	Evaluate how vitamin D and omega-3 supplements effects biomarkers of oxidative stress and pregnancy	30 women received 1000 mg of omega 3 twice a day and a vitamin D placebo, 30 women received	• Those who received both supplements had a statistically significant decrease in hs-CRP and

			outcomes in gestational diabetes	50,000 IU of vitamin D every 2 weeks and an omega-3 placebo, 30 women received 50,000 IU of vitamin D every 2 weeks and 1000 mg of omega-3 twice a day, and 30 women received both placebos for 6 weeks	MDA and an increase in total antioxidant capacity and glutathione • Combined supplementation worked better than a single supplement alone
Rodrigues et al.	2017	78 women	Evaluate how delta amniolevulinate dehydrase (δ-ALA-D) and biomarkers of oxidative stress differ in women with gestational diabetes	48 women diagnosed with gestational diabetes and 30 women in the control group gave blood samples after an 8-hour fasting period to test δ-ALA-D, protein thiol, CAT, and vitamin C levels	• Women with gestational diabetes showed a significant decrease in δ-ALA-D activity, lower vitamin C and CAT levels, and plasma levels of thiol were increased • Low δ-ALA-D are related to increased oxidative stress
Rueangdetnarong et al.	2018	62 women	Compare the levels of the biomarkers of oxidative	Blood samples were taken at 24-28 weeks'	• Blood samples from women with

			stress in women with gestational diabetes with those who were not diagnosed	gestation and when they were admitted for delivery and were measured for TNFα, IL-10, and 8IsoP levels, 32 women were diagnosed with gestational diabetes and 32 were in the control group	gestational diabetes had increased levels of 8Isop and TNFα when compared to the control • There was not a significant difference in IL-10 levels between the two groups
Saifi et al.	2019	180 women	Determine the effects of selenium supplementation on fasting plasma glucose levels and biomarkers of oxidative stress in women with gestational diabetes	60 women were given 50 mg of selenium daily for 12 weeks, 60 women were given a placebo, 60 women in good health were used as control	• Those who received the supplement showed a significant decrease in their fasting glucose levels • Those receiving the supplement had levels of plasma MDA and antioxidant levels comparable to the healthy women
Seider et al.	2018	43 women	Determine how a low glycemic index diet influences oxidative stress in	All women provided blood samples at a baseline, 4-6 weeks after dietary	• Oxidized LDL was decreased in those with a low glycemic diet

			women with gestational diabetes	intervention, and then at 4-6 months post-partum to look at biomarkers of stress	• A low glycemic diet decreases oxidative stress
Schliefsteiner et al.	2017	50 women	Determine how lipoprotein-associated phospholipase A2 (LpPLA2) activity effects oxidative stress with gestational diabetes	12 women gave placental tissue samples, 21 women gave neonatal cord plasma, and 17 women gave blood samples for Hoffbauer cell isolation to test LpPLA2 levels	• LpPLA2 levels were higher in the control group than those with gestational diabetes • HDL associated LpPLA2 activity was higher in those with gestational diabetes which in turn had an anti-inflammatory effect
Sudharshana et al.	2018	60 women	Determine how oxidative biomarkers effect correlate with women who are diagnosed with gestational diabetes	30 women were diagnosed with gestational diabetes and 30 were in the control group and blood was taken to evaluate TNFα, uric acid, and interleukin 6 levels	• TNFα and uric acid levels were significantly increased in women with gestational diabetes

Discussion

Gestational diabetes is a disease process that affects 2 to 10% of pregnancies yearly. Based on the findings of recent literature, there is a close relationship between gestational diabetes and stress. The use of many supplements to decreased oxidative stress have been studied, including probiotics, vitamin D, vitamin E, vitamin C, omega 3, selenium, calcium, magnesium, and zinc. Common stress markers tested among the studies were blood levels of hs-CRP, MDA, glutathione, and fasting blood glucose. Each study came to the conclusion that the intervention or supplement they were testing resulted in decreased oxidative stress when compared to a placebo or control group of healthy individuals, further studies should be done to compare the interventions. This could help determine which supplement or group of supplements would be best to recommend when women are diagnosed with gestational diabetes. For example, a study could also be done to determine if a specific diet, supplements, or a combination of the two works best to decrease oxidative stress in gestational diabetes.

This literature review has its limitations. One limitation is the sample size of the studies. Fourteen of the studies had total samples size of less than 100, which means that the intervention was tested on less than 50 individuals. Studies with larger sample sizes are needed to determine if the intervention continues to show statistically significant improvement in the reduction of oxidative stress. Another possible limitation is the age of participants. These studies included women between the ages of 18 and 40 years old. The health behaviors of individuals vary across this age range. Therefore, studies could have been skewed if the participants were clustered in a narrow age range. Other limitations include the use of only two databases for this literature review and exclusion of non-English articles.

Throughout the completion of this literature review, gaps in the existing literature were identified. The studies published focus on the treatment of oxidative stress in those already diagnosed with gestational diabetes. There was little to no research about the reduction of stress in the prevention of gestational diabetes. From the articles included, it is shown that reduction of stress allows for some improvement in the disease process, but more research could be done to determine ways stress can be reduced prior to pregnancy or in the first trimester to decrease the number of women diagnosed with gestational diabetes.

These articles present different supplements that can decrease oxidative stress, which could influence evidence-based practice and help nurses educate their patients. Nurses can provide explanation of and rationale for supplement use to women who have been diagnosed with gestational diabetes. This could help patients to comprehend why their provider may suggest a treatment plan over another, leading to higher compliance in the care regimen and in turn, more positive outcomes for women with gestational diabetes. In conclusion, stress has a negative impact on gestational diabetes, specifically in regard to oxidative stress. Recent literature shows reduction of stress can lead to improvement in gestational diabetes and may help to prevent it, which in turn improves pregnancy outcomes.

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