Antioxidant status and circulating lipids are altered in human gestational diabetes and macrosomia

OUSSAMA GRISSA, JEAN-MARC ATÈGBO, AKADIRI YESSOUFOU, ZOUHAIR TABKA, ABDELHEDI MILED, MEHDI JERBI, KARIM L. DRAMANE, KABIROU MOUTAIROU, JOSIANE PROST, AZIZ HICHAMI, and NAIRIM AKHTAR KHAN

SOUSS, TUNISIA; DIJON, FRANCE; AND COTONOU, BÉNIN

Fetuses from mothers with gestational diabetes are at increased risk of developing neonatal macrosomia and oxidative stress. We investigated the modulation of antioxidant status and circulating lipids in gestational diabetic mothers and their macrosomic babies and in healthy age-matched pregnant women and their newborns. The serum antioxidant status was assessed by employing anti-radical resistance kit (KRL; Kirial International SA, Couternon, France) and determining levels of vitamin A, C, and E and the activity of superoxide dismutase (SOD). Circulating serum lipids were quantified, and lipid peroxidation was measured as the concentrations of serum thiobarbituric acid-reactive substances (TBARS). As compared with non-diabetic mothers, gestational diabetic women exhibited decreased levels of vitamin E and enhanced concentrations of vitamin C without any changes in vitamin A. Vitamin A and C levels did not change in macrosomic babies except vitamin E whose levels were lower in these infants than in the newborns of non-diabetic mothers. Gestational diabetes mellitus (GDM) and macrosomia were also associated with impaired SOD activities and enhanced TBARS levels. Globally, total serum antioxidant defense status in diabetic mothers and their macrosomic babies was diminished as compared with control subjects. Triglyceride and cholesterol concentrations did not differ significantly between gestational diabetic and control mothers; however, macrosomia was associated with enhanced plasma cholesterol and triglyceride levels. These results suggest that human GDM and macrosomia are associated with downregulation of antioxidant status, and macrosomic infants also exhibit altered lipid metabolism. (Translational Research 2007;150:164–171)

Abbreviations: BMI = body mass index; GDM = gestational diabetes mellitus; GSH = glutathione; PUFA = peroxidized polyunsaturated fatty acid; RBC = red blood cell; RT = retention time; SD = standard deviation; SOD = superoxide dismutase; TBARS = thiobarbituric acid-reactive substances

G estational diabetes mellitus (GDM) is the most frequent metabolic disorder of pregnancy, occurring in 1% to 10% of all pregnancies.1 As far as the African subcontinent is concerned, Djrolo et al2 have observed a prevalence of 5.2% of GDM in Beninese women with a high tendency of cesarean delivery. Similarly, a study con-
ducted in Tunisia by Khrouf et al.\(^3\) has shown an incidence of 7.75% of GDM. The major complications of GDM include maternal hypertensive disorders, neonatal hypoglycemia, jaundice and birth trauma including shoulder dystocia.\(^4\) Although great controversy exists regarding the clinical outcome of GDM,\(^5\) it is clear that several morbidities occur with an increased frequency in offspring of gestational diabetic mothers. The most commonly reported effect on the newborn is macrosomia, which is usually defined as birth weight above either 4 kg or birth weight above the 95th percentile for the gestational age. Available evidence indicates an association between maternal hyperglycemia during pregnancy and childhood obesity.\(^6\) In fact, several alterations in carbohydrate and lipid metabolism are also observed in infants of diabetic mothers and are thought to be a consequence of maternal hyperglycemia leading to fetal hyperglycemia and hyperinsulinemia.\(^7,9\) High blood glucose levels in these newborns induce oxidative stress, which in turn evokes the production of highly reactive oxygen radicals, toxic to cells, particularly to the plasma membranes where these radicals interact with the lipid bilayer.\(^10\)

For assessing the global antioxidant status, 3 major approaches have been employed: (1) determination of endogenous antioxidant levels, (2) measurement of the products of oxidized macromolecules (lipids, DNA, and proteins), and (3) direct detection of free radicals. Assessments of lipid peroxidation by free radicals include the analysis of lipid peroxides, isoprostanes, diene conjugates, and breakdown products of lipids (eg, malonaldehyde, ethane, pentane, and 4-hydroxynonenal).\(^11\) Among these products, malonaldehyde is often used as a reliable marker of lipid peroxidation assessed by measuring the thiobarbituric acid-reactive substances (TBARS), although this assay lacks the specificity.\(^12\)

The biological effects of free radicals are normally controlled in vivo by a wide range of antioxidants, such as vitamin A, C, and E, glutathione (GSH), and antioxidant enzymes, such as superoxide dismutase (SOD), catalase, GSH peroxidase, and GSH reductase. Vitamin E, the main liposoluble antioxidant in human beings, scavenges peroxyl-radicals produced during lipid peroxidation.\(^13\) Vitamin E can transfer its phenolic hydrogen to a peroxyl free radical of a peroxidized polyunsaturated fatty acid (PUFA), thereby breaking the radical chain reaction and preventing the peroxidation of PUFA in cellular and subcellular membrane phospholipids. Vitamin A and C also have the ability to react directly with reactive oxygen species. Among antioxidant enzymes, SOD is a unique and valuable asset as a biological tool to explore reaction mechanisms. SOD inhibits radical reactions, which leads to oxidative damage, and prevents reduction of iron ions by superoxide.\(^12\) The development of biochemical techniques permitted scientists to quickly identify the isoforms of SOD like MnSOD, CuZnSOD, and FeSOD. Nitric oxide radical provided the next clue as to how SOD might be playing a critical biological role. Cu-containing or Zn-containing superoxide dismutase (ie, SOD1, the major SOD in mammalian cells) catalyzes the dismutation of superoxide anion (O\(^2^-\)) into H\(_2\)O\(_2\) and O\(_2\)\(^-\) and is an important antioxidant defense system.\(^16\) A coproduct of SOD is H\(_2\)O\(_2\), which is converted to H\(_2\)O by catalase and the selenium-dependent GSH peroxidase. Lipid hydroperoxides are detoxified to alcohols by GSH peroxidase. Another type of GSH peroxidase (phospholipid peroxide GSH peroxidase) acts on phospholipid peroxides in membrane structures.\(^11\)

To our knowledge, no study has directly investigated the antioxidant status in macrosomia and GDM. As one cause of macrosomia is GDM, and the hyperglycemia in GDM mothers may lead to increased oxidative stress, we hypothesized that macrosomic infants would, at birth, exhibit a decreased antioxidant defense, which could cause metabolic disorders during their adulthood. Therefore, it was thought worthwhile to undertake the current study to evaluate the antioxidant status of macrosomic babies born to gestational diabetic women. Glucose, insulin, and serum lipids were also investigated to characterize the diabetic state of pregnant subjects and their babies.

**MATERIALS AND METHODS**

**Subjects.** A total of 59 gestational diabetic mothers with their respective macrosomic babies were recruited in the Department of Gynaecology, Farhat Hached University Hospital, Tunisia. Medical records were screened by specialist clinicians. In GDM patients, diabetes appeared at second or third trimester of pregnancy as determined by oral glucose tolerance test according to the World Health Organization criteria. These ladies were between 19 and 42 years old. In total, 75% of the diabetic mothers had an episiotomy during delivery. They were hyperglycemic and hyperinsulinemic at the diagnosis of the disease. As control subjects, 60 healthy age-matched pregnant women and their newborn babies were selected.

Newborns were immediately weighed after delivery. Babies from diabetic mothers whose birth weight was 2 standard deviations (SDs) greater than the mean birth weight of the control infants were considered as macrosomic infants and included in the study. The mean birth weight of macrosomic babies, in this study, was 4.35 \(\pm\) 0.06 kg, whereas that of control infants was 3.22 \(\pm\) 0.08 kg with a respective body mass index (BMI) of 33.84 \(\pm\) 0.65 kg/m\(^2\) and 13.38 \(\pm\) 0.22 kg/m\(^2\).

Selected control women had no significant history of illness, no pregnancy-related complications, and no risk factor
for gestational diabetes, including normal glucose tolerance tests during the first and third trimesters of pregnancy. An attempt was made to match these women to diabetic subjects, at least regarding maternal age, BMI as determined by the weight and height of patients, parity, gestational age, and mode of delivery. Both diabetic and control mothers were offered regular examinations of their offspring. The characteristics of mothers and newborns are shown in Table I.

This study was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association and was approved by the Sousse Farhat Hached Hospital Committee for Research on Human Subjects (Tunisia). Informed written consent was obtained from all subjects. Our experimental protocol conforms to the relevant ethical guidelines for human research.

**Blood samples.** From each gestational diabetic or control mother, fasting venous blood samples were collected, at the third trimester of pregnancy, in tubes either containing or not containing ethylenediaminetetraacetic acid to obtain plasma and serum, respectively. The blood samples of the babies were collected at delivery. Serum or plasma was obtained by centrifugation (1000 g × 20 min). Plasma was immediately used for glucose determinations. Serum was aliquoted and frozen at −80°C for further determinations of vitamins, insulin, lipid concentrations, and total antioxidant status.

After removal of plasma, erythrocytes were washed 3 times with 2 volumes of isotonic saline (NaCl 0.9%, vol/vol). Erythrocytes were lysed with cold distilled water (1/4, vol/vol), stored in refrigerator at 4°C for 15 min, and the cell debris was removed by centrifugation (2000 g × 15 min). Erythrocyte lysates were assayed to determine superoxide dismutase activity.

**Determination of plasma glucose, serum insulin, and lipid concentrations.** Serum triglycerides and total cholesterol and free-cholesterol concentrations were determined by using enzymatic methods, according to the instructions furnished with the kit (Boehringer, Mannheim, Germany). Plasma fasting glucose was determined by glucose oxidase method using a glucose analyzer (Beckman Instruments, Fullerton, Calif). Serum concentrations of insulin were determined by using Insulin IRMA kit (Ref IM3210; Immunotech, Beckman Coulter Inc) with a detection limit of 0.5 µIU/mL.

The interassay coefficient of variability was 3.3% and 4%, respectively, for the concentrations 13 IU/mL and 54 IU/mL.

**Determination of vitamins A and E levels.** Serum α-tocopherol (vitamin E) and retinol (vitamin A) were extracted by hexane, dried under nitrogen, resuspended in methanol, and then quantified by reverse-phase high-performance liquid chromatography. The stationary phase was constituted of greffed silica (C18 column, HP ODS Hypersil C18; 200 mm × 4.6 mm; Lara spiral, maintenance temperature of analytical column, 35°C). The mobile phase was a mixture of methanol/water (98/2, vol/vol) at a flow rate of 1 mL/min. This method was used to quantify both vitamins A and E in a single chromatographic run in the presence of an internal standard, Tocol (Lara Spiral, Couternon, France), which was added to the samples before hexane extraction. The retention time (RT) of vitamins was determined by injection of the authentic standard of vitamin A (RT around 5 min), Tocol (RT around 8 min), and vitamin E (RT around 15 min). The peaks were detected by an ultraviolet detector set at 292 nm for vitamin E and Tocol and at 325 nm for vitamin A.

**Determination of vitamin C levels.** Total ascorbate (vitamin C) concentrations were determined in serum using the method of Roe and Kuether. After protein precipitation with 10% trichloroacetic acid and centrifugation, the supernatant (500 µL) was mixed with 100 µL of DTC reagent (9N sulfuric acid containing 2.4-dinitrophenylhydrazine 3%, thiourea 0.4%, and copper sulfate 0.05%) and incubated at 37°C for 3 h. After the addition of 750 µL of 65% (vol/vol) sulfuric acid, the absorbency was recorded at 520 nm.

**Determination of erythrocyte SOD activity.** Erythrocyte superoxide dismutase (SOD EC 1.15.1.1) activity was determined using Ransod kit (Randox, Crumlin, United Kingdom) on a Ra-50 spectrophotometer (Beckman, France). For SOD activity, xanthine and xanthine oxidase were used to generate superoxide radicals reacting with 2-(4-iodophenyl)-3-(4-nitropheno)-5 phenyl tetrazolium chloride to form a red formazan dye. SOD activity was then measured at 505 nm by the degree of inhibition of the reaction of washed hemolysed erythrocyte lysates assayed to determine superoxide dismutase activity.

| Table I. Characteristics of mothers and their offspring |
|-----------------|-----------------|-----------------|-----------------|
|                 | Mothers          | Newborns         |                 |
|                 | Control          | Diabetic         | Control         | Macrosomic      |
| Number          | 60              | 59              | 60              | 59              |
| Female/male ratio | 60/0          | 59/0            | 31/29           | 36/33           |
| Age (month/years) | 19–42 years   | 22–42 years     | <1 month        | <1 month        |
| Body weight (kg) |                 |                 | 3.22 ± 0.08     | 4.05 ± 0.06*    |
| BMI (kg/m²)     |                 |                 | 13.38 ± 0.22    | 33.84 ± 0.65*   |
| Cranial perimeter (cm) |           |                 | 34.17 ± 0.21    | 35.87 ± 0.29    |
| Macrosomia history (%) |           |                 |                 |                 |
| Episiotomy (%)  | 35              | 43              |                 |                 |
| Fasting glucose (mmol/L) | 4.86 ± 0.71   | 6.87 ± 0.63*    | 5.51 ± 0.38     | 4.99 ± 0.38     |
| Insulinemia (µIU/mL) | 5.98 ± 1.13   | 11.41 ± 4.71*   | 5.77 ± 0.88     | 7.78 ± 3.15*    |

Note: Values are means ± SDs.
*Significant difference between diabetic mothers or macrosomic newborns and their corresponding controls is as follows: P < 0.01.
erythrocytes with 2 mL of cold double-distilled water. One unit of SOD activity, expressed per gram of hemoglobin present in erythrocytes, is defined as the amount of the enzyme that gives an inhibition percentage (from 20% to 50%) of the erythrocyte hemolysis reaction.

**Determinant of serum TBARS.** Serum lipid peroxidation by free radical was determined by specifically measuring the TBARS assay in serum according to a modified method of Quintanilha et al.20 Serum was added with the trichloroacetic acid, thiobarbituric acid, and hydrochloric acid (15% wt/vol, 0.375% wt/vol, 0.25 M vol/vol, respectively) and butylated hydroxytoluen (2% in ethanol, vol/vol). After 30 min of incubation at 80°C, the tubes were allowed for cooling. After centrifugation (3000 g 10 min, 4°C), the supernatant was obtained and the absorbance measurement was made at 535 nm. TBARS were expressed as μmol of malondialdehyde per liter of serum (μM).

**Serum antioxidant defense.** Serum resistance to free radical aggression was tested as the capacity of red blood cell (RBC) to withstand free radical-induced hemolysis and was measured as per method of Blache and Prost,21 who have clearly demonstrated that, if at least 1 component of the antiradical detoxification system (antioxidants, enzymes) is impaired, a shift of the hemolysis curve is observed toward shorter times. Briefly, washed RBCs were diluted (1:40, vol/vol) with anti-radical resistance [Kit Radicaux Libres (KRL; Kirial International SA, Couternon, France)] buffer (300 mosm/L) and 50 μL of RBCs suspension was assayed in a 96-well microplate coated with a free radical generator (GRL, Kirial International SA). The kinetic of RBCs resistance to hemolysis was determined at 37°C by continuous monitoring of changes in absorbance at 620 nm. The time to reach 50% of total hemolysis was retained for group comparisons.

**Statistical analysis.** Values are mean ± SD. Statistical analysis of data was carried out using STATISTICA (version 4.1; Stat-soft, Paris, France). Data were evaluated by analysis of variance. The Duncan multiple-range test was employed for the comparison between gestational diabetic patients or macroscopic newborns and their corresponding controls. Differences were considered significant when P < 0.05.

**RESULTS**

**Serum vitamins A, C, and E levels.** As compared with non-diabetic mothers and their children, gestational diabetic women and their macroscopic newborns exhibited no significant changes in vitamin A concentrations (Fig 1). However, vitamin E levels were significantly decreased in gestational diabetic patients and their overweight babies compared with their corresponding controls (Fig 1). Vitamin C concentrations did not significantly differ between macroscopic newborns and control infants, although differences were noticed between their mothers with significant increased levels in gestational diabetic women (Fig 2).

**Antioxidant enzyme (SOD) activity.** Erythrocyte SOD activity was significantly reduced in macroscopic babies compared with that in control infants. Similarly, gestational diabetic mothers showed a lower level of SOD activity than control mothers (Fig 3).

**Serum lipid levels.** Triglyceride and total-cholesterol did not differ between gestational diabetic and control mothers. Free-cholesterol was lower in diabetic mothers than control mothers. Triglyceride, total-cholesterol, and free-cholesterol were significantly higher in macroscopic babies compared with control offspring (Table II).

**Serum TBARS concentrations.** Concentrations of serum TBARS were higher in gestational diabetic mothers and their macroscopic babies than control healthy women and their newborns (Fig 4).
Serum antioxidant capacity. Gestational diabetic mothers, as well as their macrosomic newborns, showed a significant decrease in total serum antioxidant defense compared with control mothers and their babies, respectively (Fig 5).

**DISCUSSION**

The role of oxidative stress in diabetes mellitus has been well investigated. However, no data are available on the antioxidant status in macrosomic infants born to gestational diabetic mothers, although diabetic pregnancy represents an important risk factor for fetal overnutrition and development of obesity in the offspring at adulthood. As regards the newborns of GDM mothers that were not macrosomic, we would like to mention that all subjects were recruited in Tunisia and the experimental study was performed in France. Only the macrosomic infants of GDM mothers were selected and included in the study. Unfortunately, we do not have any data regarding the non-macrosomic babies born to GDM mothers. However, we have previously observed in another study, performed on gestational diabetic rats, that the normal-sized offspring (non-macrosomic) of diabetic dams were neither hyperglycemic nor hyperinsulinemic at birth. They had normal growth rates and did not show any significant difference from control pups as far as the lipid metabolism is concerned (unpublished results). In the current study, GDM and macrosomia were found associated with a decreased level of vitamin E without any changes in vitamin A levels. In addition, vitamin C levels were increased in gestational diabetic mothers, without any significant modifications in their macrosomic offspring compared with respective control subjects. There have been conflicting reports on plasma vitamin concentrations in diabetes mellitus. Yessoufou et al have shown, in type 2 diabetic patients, diminished vitamin E levels. On the other hand, Makimattila et al have reported that plasma vitamins C and E levels in type 2 diabetic patients were not significantly decreased. Sundarm et al have reported low levels of vitamins E and C in diabetic patients. However, the findings of the current study are in close agreement with those obtained by Peuchant et al who have observed that plasma levels of vitamin E were significantly lower in pregnant women with GDM compared with control subjects, without any changes in vitamin A. We have previously suggested that the decreased level of vitamin E could be from its high utilization rate as this vitamin may be used to protect against oxidative stress. It has been established that oxidative stress is induced by both the increases in free radicals and the disturbance in the free radical scavenging system in diabetes mellitus. The inverse correlation between a decreased level of vitamin E and a high level of vitamin C, in GDM mothers, may be because vitamin C and reduced glutathione regenerate vitamin E. Low levels of vitamin E are correlated with hyperglycemia in GDM mothers. It has been reported that chronic hyperglycemia may increase oxidative stress, which may account for low vitamin E levels. In addition, diminished vitamin E levels have also been observed in diabetic patients with increased lipid peroxidation products associated with hypertriglyceridaemia. In the current study, the high level of vitamin C in GDM mothers may be caused by hyperglycemia in these subjects. Indeed, it has been shown that L-ascorbate (vitamin C) is synthesized from glucose by the D-glucuronic acid pathway in mammals.

As far as the antioxidant enzymes are concerned, the current study showed that SOD activity decreased in gestational diabetic mothers and their macrosomic offspring compared with healthy controls. Our results are in accordance with those obtained by other investigators in human beings and experimental studies. Biri et al and Chaudhari et al have observed an impaired SOD activity in pregnant women with GDM compared with normal pregnant women. Similar results have been observed by Peuchant et al who have shown a decreased SOD activity in gestational and type 1 diabetic pregnant women. Other investigators have also noticed decreased SOD activity in human type 2 diabetic compared with controls. We have also observed a decrease in SOD activity in diabetic rats and their macrosomic offspring. Dincer et al have observed a diminished SOD activity in liver and lung of neonate
streptozotocin-induced diabetic rats. However, Aydin et al. have reported that SOD activity increased in type 2 diabetes compared with controls. Ruiz et al. did not observe any significant difference in SOD activity in type 1 diabetes compared with controls. The reason for this discrepancy in SOD activity in diabetes might be attributed to the treatments given to the patients, the associated complications, and the duration of the disease. As far as SOD activity in macrosomia is concerned, only one study has shown diminished SOD activity in infants born to gestational diabetic mothers and our results are substantiated by this report.43

Gestational diabetic as well as control pregnant mothers, in the current study, exhibited hypertriglyceridemia and hypercholesterolemia, although these parameters were not statistically different. However, macrosomic babies showed high levels of serum triglyceride and total and free cholesterol compared with control infants. Our results corroborate several studies that have shown that total cholesterol and triglyceride are increased significantly throughout pregnancy and that no significant difference exists between healthy and diabetic women.44,45

Table II. Serum lipid concentrations

<table>
<thead>
<tr>
<th>Serum lipids</th>
<th>Mothers</th>
<th>Newborns</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control n = 60</td>
<td>Diabetic n = 59</td>
</tr>
<tr>
<td>Triglycerides (mM)</td>
<td>3.07 ± 0.22</td>
<td>3.07 ± 0.25</td>
</tr>
<tr>
<td>Total-cholesterol (mM)</td>
<td>6.33 ± 0.32</td>
<td>5.37 ± 0.65</td>
</tr>
<tr>
<td>Free-cholesterol (mM)</td>
<td>12.11 ± 0.34</td>
<td>9.30 ± 0.93*</td>
</tr>
</tbody>
</table>

Note: Values are means ± SDs.
*Significant difference between diabetic mothers or macrosomic newborns and their corresponding controls is as follows: P < 0.05.

Fig 4. Serum TBARS concentrations. Serum TBARS concentrations were determined as described in the Materials and Methods section. Values are means ± SDs. n = 60 control mothers/babies; n = 59 diabetic mothers/macrosomic babies. Each value represents the mean of 3 determinations. Significant difference between diabetic mothers or macrosomic newborns and their corresponding controls is as follows: P < 0.001.

Fig 5. Total serum antioxidant defense in control and diabetic women and their newborns. Serum total antioxidant defense was determined as described in the Materials and Methods section. Values are means ± SDs. n = 60 control mothers/babies; n = 59 diabetic mothers/macrosomic babies. Each value represents the mean of 3 determinations. Significant difference between diabetic mothers or macrosomic newborns and their corresponding controls is as follows: P < 0.001.

High lipids and increased oxidative stress in diabetic patients might have enhanced the susceptibility of lipid peroxidation. Gestational diabetic mothers and their macrosomic offspring exhibited a significant increase in serum TBARS in accordance with the observations of several authors.46,47 Our finding implies that TBARS are one promising clinical marker of oxidative stress. Bis-Gluchowska et al. have also shown a high level of TBARS in the cord blood of newborns delivered to mothers with type 1 diabetes, which suggests that maternal diabetes during pregnancy may induce oxidative stress in the newborn. On the other hand, Mazzanti et al. have reported that basal levels of peroxidation of the platelet membranes and TBARS levels were increased in GDM patients in comparison with control subjects; hence, oxidative stress in GDM women might be involved in cellular dysfunction. In fact, lipid peroxidation has been involved in a variety of physiological, pathological, and clinical conditions, including pregnancy-related complications, mainly in preeclampsia and diabetes.47
Our report is the first one on antioxidant status in macrosomia related to human GDM. The altered antioxidant defense observed in these macrosomic infants at birth could cause metabolic disorders during their adulthood. Indeed, we have previously reported, in rats, the potential long-term consequences of the altered antioxidant status in macrosomic offspring born to diabetic dams. Hence, the antioxidant status of macrosomic offspring, during adulthood, remained low. At 2 and 3 months of age, they exhibited (1) hyperglycemia and hyperinsulinemia, (2) high plasma TBRAS levels, (3) diminished plasma oxygen radical absorbance capacity that reflects the low antioxidant defense, (4) low vitamins C and A concentrations, and (5) the decreased activities of SOD and other antioxidant enzymes like glutathione peroxidase and glutathione as compared with the control adult offspring. Other investigators have also shown in human macrosomic infants that macrosomia was associated with alterations in lipoprotein compositions and concentrations at birth, and some of them persisted even after 1 month of life; hence, they might play a role in the pathogenesis of diabetes and atherosclerosis at adulthood. These investigators also reported that macrosomic newborns as compared with controls had higher serum lipids, apolipoprotein A-I and B-100, and lipoprotein (very low-density lipoprotein, low-density lipoprotein, high-density lipoprotein-2, and high-density lipoprotein-3) levels. By keeping in view these alterations, one can envisage the complementary therapies with antioxidants, including vitamins that might protect the organism against the production of free radicals and the decrease in antioxidant capacity. Such treatments may be beneficial in women at risk of GDM.

REFERENCES


