Effect of probiotics on quality of life and depression in pregnant women with gestational diabetes: A randomized double-blinded clinical trial

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Abstract

Background & Aims: Women are vulnerable and face variety of problems during pregnancy that can affect mental health and life quality. Pregnancy complications make pregnant women more prone to loss of quality of life and mental health problems. The purpose of this study was to investigate the effect of probiotic supplement on quality of life and depression in women with gestational diabetes mellitus (GDM).

Materials & Methods: In this double blind randomized clinical trial, performed on pregnant women with GDM referring to the specialized centers of gynecology and endocrinology in Tabriz, 64 pregnant women with GDM in 24-28 weeks of pregnancy were randomly assigned to receive either probiotic supplementation or placebo for 8 weeks. Probiotic supplement was a combination of four strains of Lactobacillus acidophilus, Bifidobacterium, Streptococcus thermophilus and Lactobacillus delbrueckii subsp. bulgaricus. The short form of Iranian species of World Health Organization Quality of Life Questionnaire was used to assess the quality of life and the Edinburgh Depression Inventory to assess depression before and after intervention.

Results: Fifty six surveyed individuals completed the study. The effect of probiotic supplementation on changes in the physical dimension of quality of life was significant, with statistically remarkable increase of 2.59 ± 2.19 units in the probiotic group compared with 2.25 ± 0.88 decrease in the placebo group (p = 0.045). Also, the increase in mean of total quality of life in the probiotic group was 5.17 ± 1.46 units which was significant compared with 0.46 ± 1.61 units increase in the placebo group (p = 0.029). The effect of probiotic supplementation in comparison with placebo was significant in improving depression (p = 0.042).

Conclusions: It seems that probiotic supplementation promotes quality of life and depression levels in pregnant women with GDM.

Registration number in Iranian Registry of Clinical Trials: IRCT201405181597N3

Keywords: Gestational diabetes mellitus, Probiotic, Quality of life, Depression

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Introduction

Gestational diabetes mellitus (GDM) is one of the most common metabolic diseases during pregnancy and affects about 7% (18-18%) of all pregnancies (1, 2). During pregnancy, organic and hormonal changes affect the physical and mental health of women. These changes can change the understanding of pregnant women about quality of life (3). Women during pregnancy face new problems that can affect their mental health and quality of life. Quality of life is a related clinical concept that expresses the individual assessment of her health status. This mental assessment seems to affect most of all the physical and therapeutic components of diabetes during the period of diabetes as a psychological factor contributing in medical outcomes during GDM. According to recent research, quality of life is significantly affected in short and long term in women with GDM, and efforts to promote quality of life play an important role in the individuals’ health (4). According to studies, GDM reduces the quality of life (5) and the health status of pregnant women (6) and leads to depression during pregnancy (7, 8) and later (6).

On the other hand, according to Henkel et al., pregnant women with depression in the first trimester are twice as likely to develop GDM. Pregnant women with depression symptoms, as compared with non-depressed pregnant women, cannot receive proper care during pregnancy due to reduced motivation (9). Lack of depression treatment has long-term negative consequences for women and could have negative impact on maternity role, mother-child relationship, child development and marital relationship (10).

Some researchers believe that decreasing of beta cell function and insulin is associated with sensitivity with biomarkers such as leptin, adiponectin, resistin, or changes in non-stylistic fatty acids (11, 12). In addition, these biomarkers undergo significant changes in psychiatric disorders, including major depression (13, 14).

Nutritional factors during pregnancy can trigger a cascade of metabolic and inflammatory-immune cycles that could be found in later stages of life (15). One of these factors is gut microbiota. Specific probiotic interventions are aimed at correcting and normalizing the characteristics of the native microbial population, intestinal duct function and immune regulation for better control of local and systemic inflammation (16).

Generally, at the end of pregnancy, the number of proteobacteria and acinetobacteria increases and bacterial enrichment is reduced (17). These changes have the ability to modify the immune system to facilitate metabolic and immunological adaptation (17, 18). Recently, due to the importance of the intestinal microbial population in the development of diseases associated with dysbiosis, increasing microbiota-suppressive therapies are provided, including the use of probiotics (19, 20). Probiotics are living microorganisms colonized in the gastrointestinal tract and affect various pathways, and are available as supplement in the form of tablets or powder.

Regarding the effect of probiotic supplementation on quality of life or depression and behavioral disorders, many studies have been conducted in non-pregnant populations. In a double-blind randomized clinical trial in patients with irritable bowel syndrome, administering probiotic Bifidobacterium lungum NCC3001 for 6 weeks resulted in a 2-degree or greater reduction in depression score in 64% of supplemented subjects. This rate in placebo group was 32%. However, this supplementation did not have a significant effect on the anxiety score of the participants (21).

According to studies, women with a history of spontaneous miscarriages or the birth of a dead baby compared with women who do not have such a case, have a lower quality of life in their later pregnancies (22). According to recent study results, older women during their child birth have higher quality of life related to health, and moreover, the number of previous pregnancies with live birth is an important factor in determining that as the individual's age at the time of the first child's birth is higher, the life quality associated with greater health is higher (23). In other studies (24, 25) multiparous women, particularly with higher ages, have more depression than nulliparous, and women who are pregnant for the first time are more anxious than women for the second time, both during pregnancy and
postpartum period. These results indicate the possibility of parity role along with other factors in depression and life quality.

Concerning the use of probiotics in GDM and the effect on the metabolic profile of pregnant women, several clinical trials have been conducted (26-28) and promising results have been obtained. However, there has been no study on the effects of probiotic supplementation on depression and quality of life in pregnant women with GDM. In this study, first the effects of probiotic supplementation of Lactobacillus acidophilus LA-5, Bifidobacterium BB-12, Streptococcus thermophilus STY-31 and Lactobacillus delbrueckii subsp. bulgaricus LBY-27 on quality of life and depression was investigated in pregnant women with GDM.

Materials & Methods

Study design and participants:
This randomized, double-blinded, placebo-controlled clinical trial lasted for 8 weeks. It has been registered with the Iranian Registry of Clinical Trials (http://www.iret.ir; IRCT201405181597N3). Women with the first pregnancy and diagnosis of GDM in screening of 24-28 weeks of gestation referred to specialized gynecology and endocrinology centers of Tabriz, enrolled in this trial from Feb 2014 to Sep 2014. The study protocol was approved by the ethics committee of the Shahid Beheshti University of Medical Sciences and informed consent forms were signed by all participants prior to the intervention. The subjects were selected through convenient sampling from patients with GDM according to inclusion and exclusion criteria. The criteria for entering the study included: the first pregnancy, diagnosis of GDM with a single-stage oral glucose tolerance test with 75 g oral glucose (OGTT) between 24 weeks and 0 days, and 28 weeks and 6 days of gestation with a specialist screening test, age group of 18 to 45, fasting blood glucose between 92 to 126 mg/dl at the time of diagnosis, body mass index of 18.5 and above, no history of type 2 diabetes, no chronic illness, no smoking, alcohol, no use of probiotics from 2 weeks before the start of the intervention, no taking of antibiotics within one month before and during the study, and no acute gastrointestinal problem during a month from the beginning and throughout the study. Exclusion criteria include the need for insulin and other hypoglycemic agents and their use during the study.

Study procedures:
The design of the study is detailed in another article by the author (26). A total of 84 patients with diagnosis of GDM were screened for 24-28 weeks of gestation. To determine the sample size, the primary data including the mean and standard deviation of the quality of life variable were obtained from the study by Latif et al. (2014). Considering 95% confidence interval, 80% power, two-sequence test and 1.2 as the effect size in the main variable, and using the G-power software, the minimum sample size in each group was calculated 26. With a 25% losses, the sample size was increased to 32 in each group (29). The gestational age was calculated from the data of the last menstrual period and simultaneous clinical examinations. Out of these, 20 were excluded from the study due to reluctance to continue the study or lacking entry criteria. 64 subjects were randomly assigned into two groups of 32. Of these, 5 were in the intervention group (2 due to the unwillingness to continue the study, 1 due to preterm labor, and 2 due to the need for medication) and 3 in the control group (1 due to unwillingness to continue the study, 1 due to lack of supplemental consumption and 1 due to the need for drug therapy) were excluded from the study. Finally, data from 29 subjects in the probiotic supplement group and 27 subjects in the placebo group were statistically analyzed.

At the beginning of the study, the purpose and method of the study were described in detail for the patients, and the dietary recommendations were presented in the same way by a trained nutritionist. Then, during the interview with the participants, a general information and 24-hour food recall questionnaire were completed. Subjects were randomly assigned into two group to intake one probiotic capsule (n=32) or placebo (n=32) once daily for 8 weeks. Randomization assignment was performed using the computer-generated random numbers by a trained nutritionist. 4biocap probiotic...
capsule is composed of four probiotic strains including (180 mg) of a standard powder consisting of >10^9 × 4 Lactobacillus acidophilus LA-5, Bifidobacterium BB-12, Streptococcus thermophilus STY-31 and Lactobacillus delbrueckii subsp. bulgaricus LBY-27 in addition to Dextrose Anhydrate and Lubricant Magnesium Stearate filler in Kristin Hansen of Denmark and Packaging in TehranDarou Pharmaceuticals Company protected against light and moisture with a gelatinous coating without the need to be kept in the refrigerator.

A placebo capsule was made in TehranDarou Pharmaceuticals Company with the same specifications without the above mentioned bacteria in the completely similar design, color and shape.

During the 8 weeks of the study, the subjects received daily one probiotic capsule and control group one placebo similar capsule daily after the meal.

Demographic information was collected through face-to-face interview using a general questionnaire including demographic and medical information. Individual information including age, gestational age, diabetes in first-degree relatives, pre-pregnancy weight, educational level, occupation, physical activity, follow-up of a particular diet, history of various diseases, use of antibiotics, various supplements, disease of acute gastrointestinal tract during the past month and the use of probiotic foods over the past two weeks.

The physical activity of the participants was assessed using a standard IPAQ questionnaire, with confirmed validity and reliability in Iran (30). The categorical score method was used to calculate physical activity and the participants were classified into three groups of with low physical activity, moderate physical activity and severe physical activity.

All subjects completed three dietary records (two non-consecutive week days and one weekend). Nutritionist IV software used to determine macro-and micro-nutrient intakes (31) (First Databank, San Bruno, CA, USA) modified for Iranian foods. The macronutrient and micronutrient intakes of each individual were determined for three days before, 4 weeks after the beginning and the end of the intervention for both groups.

In order to control the subjects regarding the use of supplements and prevent the loss to follow up, every week, a phone call was made with them to meet their problems and asking them about infectious and gastrointestinal diseases. At the end of every two weeks, the participants were asked to bring the capsules pouch in order to decide whether to remove them according to remaining capsules in the pouch or to maintain them in statistical analysis.

**Assessment of outcomes:**

**Assessment of life quality:**

In this study, the short form of the World Health Organization Quality of Life Assessment (WHOQOL) BREF-WHOQOL was used to assess the quality of life, which assessed the quality of life in four areas of physical health (such as daily activities, dependence on medical and treatment assistance, work capacity, sleep and rest), mental health (positive and negative emotions, self-conception, thinking, memory and learning), social relationships (personal relationships and social activities), and environmental health (financial resources, social and health care, the home environment, opportunities for receiving new information and skills and physical environment such as pollution, climate, noise and traffic), and each area has 7, 6, 3 and 8 questions, respectively. The questionnaire has a total of 26 questions and the first two questions of quality of life are evaluated in general. In each area, the obtained score can be attributed to 0-100, in which the lower score indicates the worse quality of life (32, 33). The Persian version of this questionnaire has been examined in terms of validity and validity in all four areas (32).

**Assessment of depression:**

The Edinburgh Depression Inventory was developed by Cox et al in 1978 and revised in 1994. The questionnaire has 12 questions of four choices, each with a score of 0 to 3, and a total score of between 0 and 36. The participant chooses the answers felt during the last week. The score of 12 and above indicates depression in pregnant women. Validity and reliability of this
questionnaire have been reviewed and approved in Tabriz (34).

**Statistical analysis methods:**

Data were presented as mean (± standard deviation) and frequency (percentages) for quantitative and qualitative variables, respectively. Data analysis was done by SPSS software version 17.

The normal distribution of data was evaluated using the Kolmogorov-Smirnov test. Given that the test for small sample size has the ability to detect deviation from low normality, descriptive evidence such as slip and stretch indices, and proportional and reasonable standard deviations (in comparison with the mean) were also evaluated.

To compare principal traits and dietary intake between two groups, Chi-square test and independent sample t-test were used. In order to compare the mean of the studied variables after intervention, two groups of covariance test were used. In this study, the P value was considered less than 0.05 (35).

**Ethical considerations of study:**

At the beginning of the study, the objectives of the design and method of work were explained in detail for each individual, and written informed consent was obtained from all the participants. This study was approved by the Ethics Committee of Research Vice-Chancellor of Shahid Beheshti University of Medical Sciences (License No. 449/116, dated 28/02/1393) and was registered on the Iranian website of clinical trials with IRCT201405181597N3 code.

**Results**

At the end of the study, a total of 64 nulliparous pregnant women with diagnosis of gestational diabetes mellitus participated in the study; data were analyzed for 56 subjects (29 in the complementary probiotic group and 27 in the placebo group). No side effects were reported in patients following supplemental intake (Figure 1).

The general profile of pregnant women in the study is presented separately from the groups under study in Table 1.

The mean age of the patients was 27.34 ± 5.79 years, 28.24 ± 6.24 and 26.48± 5.26 for probiotic and placebo groups, respectively, where there was no significant difference between the two groups according to the mean age.

As shown in Table 1, the two groups did not differ significantly in terms of distribution of confounding variables at the beginning of the study. There was no significant difference between two groups in terms of height, weight and body mass index (BMI). Also, the two groups were identical in terms of the variables studied at the beginning of the study.

Regarding the significant decrease in total dietary intake in both groups before, during and after intervention, to control the confounding effect of energy, macronutrient intakes and micronutrients were adjusted to total energy intake by regression analysis (residual model).

Total daily energy intake from the beginning of the study to 4 weeks after the study and then up to 8 weeks after the study in the intervention and control group decreased significantly due to the dietary recommendations presented in the same way to both groups of patients. The decrease in energy intake in both groups was similar and there was no significant difference between the two groups at baseline, during and at the end of the study (p> 0.05).

During the study, the effect of intervention on changes in the physical dimension of quality of life was significant, with a significant mean increase of 2.59± 2.19 units in the mean score of the physical health of the probiotic group compared with 2.25 ± 0.88 in the placebo group, (P = 0.045). The results didn’t confirm the probiotic supplementation effect on mental health (p = 0.068), social health (p = 0. 854) and environmental health (p = 0.246). A total quality of life score showed that the use of probiotic supplementation was significant in increasing the overall quality of life score, with a mean increase of 5.17 ± 1.46 in the mean total score of quality of life in the probiotic group versus 0.46±1.70 in the placebo group. The increase unit in the placebo group was statistically significant (p = 0.029). The use of probiotic supplementation can significantly improve depression in the intervention group, as reduction of 1.38 ± 0.42 units in the depression mean score in the probiotic group.
versus 0.26-0.53 in the placebo group was statistically significant (p = 0.042) (Table 2).

**Table 1:** Specifications of the subjects in the two groups at the time of intervention *

<table>
<thead>
<tr>
<th>Profile of pregnant mothers</th>
<th>Intervention group (n = 29)</th>
<th>Placebo group (n = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother's age (year)</td>
<td>28.14±6.24</td>
<td>26.48±5.23</td>
<td>0.36</td>
</tr>
<tr>
<td>Pregnancy age (week)</td>
<td>25.47±1.79</td>
<td>25.92±1.05</td>
<td>0.25</td>
</tr>
<tr>
<td>Family history of diabetes</td>
<td>16(55.2%)</td>
<td>12(44.4%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under diploma</td>
<td>4(13.8%)</td>
<td>5(18.5%)</td>
<td>0.89</td>
</tr>
<tr>
<td>diploma</td>
<td>17(58.6%)</td>
<td>15(55.6%)</td>
<td></td>
</tr>
<tr>
<td>academic education</td>
<td>8(27.6%)</td>
<td>7(25.9%)</td>
<td></td>
</tr>
<tr>
<td>Employment status (employed)</td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>Location (City)</td>
<td>17(58.6%)</td>
<td>15(55.6%)</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Low</td>
<td>22(75.9%)</td>
<td>17(63.0%)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>7(24.1%)</td>
<td>10(37.0%)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg / m 2)</td>
<td>31.41±3.92</td>
<td>29.86±3.39</td>
<td>0.12</td>
</tr>
<tr>
<td>Quality of Life</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical health</td>
<td>60.34±4.48</td>
<td>61.90±4.47</td>
<td>0.807</td>
</tr>
<tr>
<td>mental health</td>
<td>62.78±4.49</td>
<td>53.85±5.00</td>
<td>0.189</td>
</tr>
<tr>
<td>Community Relations</td>
<td>61.49±3.95</td>
<td>62.34±3.54</td>
<td>0.874</td>
</tr>
<tr>
<td>Environmental health</td>
<td>54.84±3.98</td>
<td>56.01±3.93</td>
<td>0.836</td>
</tr>
<tr>
<td>Depression</td>
<td>16.51±0.92</td>
<td>14.55±0.98</td>
<td>0.152</td>
</tr>
</tbody>
</table>

* To compare quantitative variables, independent t-test and for qualitative variables Chi-two have been used. The numbers of tables are for quantitative variables (standard deviation ± mean) and for qualitative variables [(percentages) of numbers].
Table 2: Comparison of mean and standard deviation of quality of life values in different dimensions and depression in two groups after intervention

<table>
<thead>
<tr>
<th>variable</th>
<th>dimensions</th>
<th>Probiotic (n=29)</th>
<th>Placebo (n=27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Physical Health</td>
<td>Before intervention</td>
<td>60.34(4.48)</td>
<td>61.90(4.47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>62.93(3.92)</td>
<td>59.65(4.27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>2.59(2.19)</td>
<td>-2.25(0.88)</td>
</tr>
<tr>
<td></td>
<td>Mental Health</td>
<td>Before intervention</td>
<td>62.78(4.49)</td>
<td>53.85(5.00)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>64.79(4.09)</td>
<td>54.32(4.44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>2.01(1.28)</td>
<td>0.46(0.98)</td>
</tr>
<tr>
<td></td>
<td>Life Quality</td>
<td>Before intervention</td>
<td>61.49(3.95)</td>
<td>62.34(3.54)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>60.91(3.53)</td>
<td>62.03(3.59)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>-0.57(1.48)</td>
<td>-0.31(1.63)</td>
</tr>
<tr>
<td></td>
<td>Social Relationships</td>
<td>Before intervention</td>
<td>54.84(3.98)</td>
<td>56.01(3.93)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>54.95(3.78)</td>
<td>57.63(3.82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>0.11(1.07)</td>
<td>1.62(1.04)</td>
</tr>
<tr>
<td></td>
<td>Environmental Health</td>
<td>Before intervention</td>
<td>50.00(3.22)</td>
<td>40.27(3.22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>55.17(3.53)</td>
<td>40.74(3.30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>5.17(1.46)</td>
<td>0.46(1.61)</td>
</tr>
<tr>
<td></td>
<td>Total Score</td>
<td>Before intervention</td>
<td>16.51(0.92)</td>
<td>14.55(0.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>15.13(0.98)</td>
<td>14.81(0.89)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Changes</td>
<td>-1.38(0.42)</td>
<td>0.26(0.53)</td>
</tr>
</tbody>
</table>

* To compare the variables after the intervention, the covariance analysis test was used.

**Discussion**

According to the results of this study, the probiotic supplementation of Lactobacillus acidophilus, Bifidobacterium, Streptococcus thermophilus and Lactobacillus delbrueckii subsp. bulgaricus for 8 weeks in pregnant women with GDM improved the physical aspect and total score of the quality of life and improved depression score in participants. Regarding our knowledge, the present study is the first one on the effects of probiotic supplementation on quality of life and depression in pregnant women with GDM.

Pregnancy is a stressful state associated with physiological and mental changes putting individual in a situation between illness and normal condition (36). The conditions become sensitive in case of GDM that requires attention and special treatments. GDM is a potential risk factor for pregnant women and fetuses and is clinically implicated with negative effects on the mental health of pregnant women, particularly their quality of life (6, 8). According to Makvandi et al. (37) study, the lowest score of life quality in pregnant women is related to the dimensions of vitality sensation and performance limitations are due to physical problems.
Mousavi and colleagues (38) also compared the quality of life and psychological status in primiparous and multiparous women, and concluded that multiparity has a negative impact on the quality of life and the psychological state of women during pregnancy. Symptoms of depression and anxiety are common in pregnancy and are associated with maternal complications and have a negative impact on the health of the baby.

Based on the results of Trutnovsky and colleagues (39), quality of life is significantly reduced in women with GDM. Particularly women with GDM from the middle to late pregnancy leading a significant reduction in the scores of physical, psychological and social scales, and the WHOQOL-BREF overall score for the quality of life.

Focusing on the quality of life in this crucial period, researchers have used various interventions to find out their impact on improving quality of life.

Considering probiotic supplementation as one of the above mentioned interventions in promoting quality of life, studies on the effects of probiotic supplementation in pregnancy on the quality of life are rare. Mirghafourvand et al. (40) examined the effects of daily intake of probiotic enriched with Lactobacillus acidophilus (La-5) and Bifidobacterium lactose (Bb-12) in pregnant women during the 24th to 28th week of pregnancy. Patients in the control group received 300 g of yogurt containing $4.8 \times 10^{10}$ units of the probiotic strains three times a day for a period of four weeks. Quality of life was evaluated before and after the study using SF-36 quality of life questionnaire. According to the results, probiotic yogurt had no significant effect on the physical and psychological aspects of life quality in pregnant women compared with normal yogurt for 4 weeks after adjusting to basal values. The results contradict the results of current study which probiotic supplementation resulted in significant improvement of life quality from physical aspect. However, the effect of probiotic supplementation on the psychological dimension was not significant in this study.

Multiple interventional studies have been conducted using various nutritional supplements to assess their impact on the improvement of depression score. However, the study on the effects of probiotic supplement or foods on the symptoms of depression in pregnancy is rare. However, several studies have been carried out on non-pregnant population. Along with the results of the present study investigating the effect of probiotic supplementation on depression score, Akkasheh and colleagues (41) randomly assigned 40 patients with depression to receive probiotic supplement containing Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum or placebo for 8 weeks. Depression was assessed using the Beck Depression Scale before and after the study. The results showed that probiotic supplementation significantly reduces Beck depression score compared with placebo and has positive results in improving the mood status of the subjects. Also, during a clinical trial, Steenbergen et al. (42) allocated 40 healthy adult women randomly to two groups of intervention and placebo. The participants in the intervention group received a probiotic supplement containing Bifidobacterium bifidum, Bifidobacterium lactis, Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus casei, Lactobacillus salivarius and Lactococcus lactis for 4 weeks. After this period, the subjects in the probiotic group had less cognitive responsiveness to the sad morality than placebo, mainly due to decreased rumination and aggressive thoughts.

Based on the results of the studies, the probiotic supplementation effects on depression and mood may be due to the regulation of inflammatory biomarkers and the neurotransmission of serotonin. It has been shown that the level of inflammatory markers increases in depression (43), which activates the hypothalamic-pituitary-adrenal axis and leads to depression. Also, inflammation can affect the metabolism of neurotransmitters. This inflammation is caused by an increase in the permeability of the intestinal barrier (44). The effect of so-called probiotic supplementation on inflammatory factors in pregnant women with GDM is mentioned in another study by this author (45). It is hypothesized that probiotics reduce general inflammation and affect the central nervous system by...
improving the integrity of the intestinal mucous membrane (51).

On the other hand, serotonin is made up from the essential amino acid, tryptophan, in the central nervous system and digestive system. It has been suggested that probiotics increase the production of tryptophan and therefore the serotonin availability. This increase in serotonin may facilitate the adjustment of hypothalamus-pituitary-adrenal axis and improve the symptoms of depression (46, 47).

In addition to above, improvements in the symptoms of gastrointestinal tract, particularly abdominal pain and bloating, are mentioned in the mechanism of the effect of probiotic supplementation and food products on the quality of life (48). According to the previous studies, patients with abdominal pain have five times less Bifidobacterium than individuals without abdominal symptoms (49). Breik et al. has concluded that the mice intestinal microbiota affects the behavioral and biochemistry of the brain, and gastrointestinal symptoms and the intestinal dysbiosis can play a role in the development of psychological disorders (50). The influence of probiotics on brain activity with more emphasis on affective and emotional domains was also shown later in human studies (51).

The present study is a first one on the effects of probiotic supplementation on quality of life and depression in pregnant women with GDM. The strength of this study is designing as randomized double-blind clinical trial. However, there are some limitations in this study, including the short duration of intervention, the lack of control of healthy pregnant women, and the limited generalization of the results of the study due to the nulliparous participants that should be considered in future studies.

**Conclusion**

The use of probiotic supplementation of Lactobacillus acidophilus, Bifidobacterium, Streptococcus thermophilus and Lactobacillus delbrueckii subsp. Bulgaricus for 8 weeks in pregnant women with GDM improves the quality of life in physical and general health areas and also reduces the scores of the depression scale and improves the mood of the participants.

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**Disclosure**

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