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Effect of Probiotics on Preventing Gestational Diabetes among High-Risk Pre-Diabetic Pregnant Women: A Randomized Controlled Trial

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Abstract

Aim: This study aimed to evaluate the effect of probiotics on preventing gestational diabetes in high-risk pregnant pre-diabetic women.

Study design: A randomized controlled trial

Place and Duration: This study was conducted at Sandeman Provincial hospital Quetta Pakistan from January 2020 to February 2021.

Methodology: In this double-blind study, 249 pregnant high-risk pre-diabetic women were included. This study comprised of 3 groups; control, intervention, and placebo. One probiotic capsule was additionally prescribed from 14 to 16 weeks of pregnancy for 12 weeks in the intervention group. In the placebo group, a placebo was prescribed for the same duration. After the prescribed duration, a glucose tolerance test was performed. Demographic and pregnancy-related data, results of diabetes tests during pregnancy, and drug history were collected. SPSS software version 23 was used to analyze the data. Chi-square test, Kruskal–Wallis one-way analysis, one-way ANOVA analysis, and Mann-Whitney U test were performed on the data. A P-value less than 0.05 was considered significant.

Results: A total of 26 % of participants in the intervention group, 60 % in the placebo group, and 67 % in the control group were diagnosed with gestational diabetes, with a p-value less than 0.001. These results showed that the participants in the intervention group had significantly fewer gestational diabetes cases as compared to placebo and control group

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participants. The Chi-square test for the comparison of diabetes between the intervention group and placebo group showed a significant difference, with a p-value less than 0.001. The Chi-square test for the comparison of diabetes between the intervention group and control group also showed a significant difference, with a p-value less than 0.001. The prevalence of gestational diabetes was significantly less in the interventional group as compared to the placebo and control group, with the p-value less than 0.05.

Conclusion: This study concluded that the usage of probiotics decreases gestational diabetes in high-risk pre-diabetic pregnant women.

Keywords: pre-diabetic, gestational diabetes, probiotic, prevention, pregnancy, blood glucose level, fasting blood glucose level.

Introduction:

One of the most common pregnancy complications is gestational diabetes globally. The prevalence of gestational diabetes has increased worldwide, which has increased the burden on the health care system [1]. Hence, coming out as one of the main concerns of the health care system [2]. During pregnancy, a high blood sugar level is called gestational diabetes [3]. About 14 to 18 percent of pregnant women are at risk of gestational diabetes [4]. It is a silent disease, which can lead to complications in pregnancy and during parturition [5].

Gestational diabetes increases the risk of congenital disorders. These women are also more prone to type II diabetes mellitus. Almost 90 % of such women are at increased risk of preeclampsia, high blood pressure, and pyelonephritis [6]. Hence, control of this disease is very important. There is no absolute treatment of gestational diabetes [7]. But lifestyle changes i.e. diet control and exercise can help control diabetes. These changes are not easy to exercise, so there is a need for proper control and prevention of diabetes. Diet counseling can also be beneficial in the management of the disease. Along with that, the use of probiotics can also be helpful [6].

Probiotics are living microbes that are beneficial for humans [8]. Bifidobacteria and lactobacilli are the probiotics that reside in the human stomach and intestine [9]. These are beneficial for human health. The factors that disturb these microorganisms i.e. stress, also disturb human health. That's why ingestion of probiotics helps keep the gut healthy and maintain microbial balance. Probiotics can also be used to reduce inflammation, control and prevent diabetes, constipation, diarrhea, irritable bowel syndrome, and lactose intolerance [10, 11, 12]. Pregnancy can affect the balance of intestinal microbes [13]. However, during the first trimester, the balance is not disturbed.

During pregnancy, almost 60 to 70 % of women experience an increase in actinobacteria and proteobacteria. Actinobacteria increase 1.8 times and proteobacteria 4.4 times. This increase is more marked in overweight women. Bacteroides and staphylococcus aureus increases more in overweight pregnant women as compared to normal-weight pregnant women. [14, 15]

Women with gestational diabetes have decreased intestinal microbes, particularly during the third trimester of pregnancy. This change affects the normal glucose metabolism by unknown mechanism [14]. The changes in gene expression and permeability of intestinal cells reduce

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glucose uptake. On the other hand, colonization of the intestine by the microbes leads to decreased blood glucose levels [6].

This study aimed to evaluate the effect of probiotics on preventing gestational diabetes in pregnant high-risk pre-diabetic women.

Methodology

This study was conducted at Sandeman Provincial hospital Quetta Pakistan from January 2020 to February 2021. In this double-blind randomized controlled trial, 249 pregnant high-risk pre-diabetic women were included. This study comprised of 3 groups; control, intervention, and placebo. Permission was taken from the ethical review committee of the institute. Proper written consent was taken from the participants and an ethical code was followed. Alpha sample size was set to 0.05 and the beta was 0.20. Inclusive criteria of this study were age older than 18 years, 14 to 16 weeks of pregnancy, no current infection, no psychological disorders, no recent use of antibiotics, no morbidities like hypertension, heart conditions, or pregnancy complications like placenta Previa, bleeding problem or chance of abortion. Exclusive criteria were an occurrence of pregnancy complications, fetal abnormalities, use of antibiotics, and discontinuation of a probiotic capsule.

Each of the three groups contained 83 women at the initial stage of the study. But as the study progressed, 4 women of the probiotic group were dropped from the study due to abortion, premature birth, and antibiotics use. A total of 2 women in the placebo group were dropped due to abortion and 2 from the control group due to premature delivery and abortion.

Participants with more than 25 kg per square meter body mass index, history of gestational diabetes, age above 40, family history of diabetes mellitus or gestational diabetes, history of macrosomia, history of the abnormal blood sugar level, polycystic ovarian syndrome, use of corticosteroids, history of miscarriage and use of antipsychotic drugs were considered at high risk of gestational diabetes [16]. In the case of first pregnancy, if fasting sugar level was between 93 to 125 mg/dL and after 14 days of diabetic diet and exercise if the fasting blood sugar was less than 95 mg/dL and sugar level after 2 hours of the meal was less than 120 mg/dL then the participant was considered as high-risk pre-diabetic.

Demographic and pregnancy-related data, results of diabetes tests during pregnancy, and drug history were collected of all the participants. The content validity method was used to determine the validity of the content. The retest method was used to evaluate the reliability of the diabetes test. Blood samples for the diabetes test were collected from 10 women, divided into 2 halves, and sent to a laboratory with different names. For the same 10 women, a glucose tolerance test was performed twice. The correlation between the results of these two test series was evaluated. The p-value was less than 0.05 and reliability, r, was 0.92.

Probiotic and placebo capsules were the same in color, packaging, and weight. 500 mg probiotic capsule was given to the intervention group daily for 12 weeks. The probiotic capsule contained Streptococcus, lactobacilli, and Bifidum. Placebo and the control group were given 500 mg capsule of starch for 12 weeks. 75 g glucose tolerance test was performed at weeks 26 to 28 on all the participants. The abnormal test result was considered equivalent

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to gestational diabetes. SPSS software version 23 was used to analyze the data. Chi-square test, Kolmogorov-Smirnov test, t-test, Fisher's test, logistic regression, and Mann-Whitney U test were performed on the data. A P-value less than 0.05 was considered significant.

Results:

The mean age of the participants was 30 years. The mean body mass index was 26 kg/m^2. A total of 8 women were dropped from the study due to abortion, premature birth, or the use of antibiotics. Hence, the final analysis was performed on 241 women. The distribution of quantitative variables was evaluated by performing the Kolmogorov-Smirnov test. The number of pregnancies, age of pregnancy, history of blood sugar levels, weight gain at the start of the study and during it, body mass index, risk assessment scores, fasting blood sugar test for a first pregnancy, fasting blood sugar at 2 weeks follow up, blood sugar level 2 hours after the meal and glucose tolerance test had abnormal distribution in all 3 groups. Age variables were normally distributed in the intervention and control group and abnormal in the placebo group. Height variables were normally distributed in the intervention group and abnormal in the placebo and control groups.

All the three groups showed almost the same outcome in the case of exercise and diabetic diet. This was statically insignificant. This is shown in Table 1.

A total of 26 % of participants in the intervention group, 60 % in the placebo group, and 67 % in the control group showed abnormal glucose tolerance tests, which marked gestational diabetes. Chi-square test results showed that the number of abnormal glucose tolerance tests was significantly different in all three groups, with the p-value less than 0.001. This is shown in Table 2. These results showed that the participants in the intervention group had significantly fewer gestational diabetes cases as compared to placebo and control group participants.

Kruskal-Wallis test showed a significant difference in the 26 to 28^{th} week of pregnancy's fasting blood sugar level after an intervention. The p-value was equal to 0.001. Hence, this index was decreased in the intervention group as compared to the control and placebo groups. Blood sugar level was tested after intake of 75g of glucose in all three groups after 1 and 2 hours. These results are shown in Table 3

Table 1: Results of diet and exercise variables in all three groups

		Intervention group	**Placebo group**	**Control group**
		Percentage	**Percentage**	**Percentage**
Pre-diabetic diet	**Yes**	89	83	84
Pre-diabetic diet	**No**	11	17	16
Pre-diabetic diet	**Total**	100	100	100
Exercise	**Yes**	91	88	80
Exercise	**No**	9	12	20
Exercise	**Total**	100	100	100

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Chi-square test result in pre-diabetic diet	p = 0.536, df = 2, X^2 = 1.23
Chi-square test result in exercise	p = 0.196, df = 2, X^2 = 3.369

Table 2: Frequency of gestational diabetes in all three groups

Glucose tolerance test	**Intervention group**	**Placebo group**	**Control group**	**Test result**
Abnormal	**Percentage**	**Percentage**	**Percentage**	
Yes	26	60	67	X^2 = 30.614
No	74	40	33	df = 2
Total	100	100	100	p = 0.001

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Table 3: Blood sugar level after 1 and 2 hours of intake of 75g of glucose in all three groups

Variable	**Intervention group**	**Placebo group**	**Control group**	**Cross-Wallis test result**
Fasting blood sugar at 26-28 week	91	95	95	X^2 = 29.387, df = 2, p = 0.001
Blood sugar level after 1 hour	153	165	167	X^2 = 23.053, df = 2, p = 0.001
Blood sugar level after 2 hours	123	117	114	X^2 = 1.96, df = 2, p = 0.379

Discussion:

In this study, probiotics proved to be effective in preventing gestational diabetes in high-risk pre-diabetic pregnant women. These results showed that the participants in the intervention group had significantly fewer gestational diabetes cases as compared to placebo and control group participants. In the same way, another study comprised of 270 obese pregnant women showed that probiotic use decreased gestational diabetes by almost 30 percent [17]. Another study reported that the prevalence of gestational diabetes reduced 3 times as compared to placebo group [18].

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One study investigated the effects of probiotics on gestational diabetes, Apgar score, and fetal development. The results showed that probiotics reduced the risk of gestational diabetes [19].

In a study, Lactobacillus and Bifidobacterium were used as probiotics from the start of 2nd trimester of the pregnancy. Glucose testing at 28 weeks showed that these probiotics did not prevent gestational diabetes [20]. The type of probiotic used in this study was different from the one used in our study. This suggested that the different types of probiotics have different effects [21]. This aspect needs further investigation. Although much research has been conducted on Lactobacilli, which revealed that different species have different probiotic effects, more research is required to know its effect in different diseases. Due to the difference in the type and quantity of probiotics used in our study and Callaway's study, the results of both the studies are not consistent [20].

In our study, Streptococcus, Lactobacillus, and Bifidobacterium probiotics were used for 12 weeks. In another study, probiotic capsule contained Bifidobacterium bruh, Bifidobacterium infandis, Streptococcus thermophiles, Lactobacillus delbrueckii, Lactobacillus Plantarum, Bifidobacterium longum, Lactobacillus paracasis, and Lactobacillus acidophilus [22]. The effect of this probiotic capsule in preventing gestational diabetes was evaluated in 82 pregnant women. The results showed no significant effect, fasting blood sugar levels did not decrease. The difference in the results of this study and our study can be due to the difference in the type of probiotics used. The sample size of this study was also small compared to ours. Other differences included the difference in gestational age and duration of intervention. Jafarnejad's study included women with gestation periods from 24 to 28 weeks and the probiotic capsule was given for 8 weeks only [22]. On the other hand, in our study, the gestation age of women was 14 to 16 weeks and the capsule was given for 12 weeks. Jafarnejad's study divided the participants into 2 groups while in our study there were 3 groups.

The strengths of our study include a random selection of intervention, placebo, and control groups, and dividing the research samples into three groups. Also, selecting appropriate gestational age to include the participants. One of the shortcomings of this study was that we did not do stool testing to ensure consistent microbial mass in the intestine. To improve the results of this study, the sample size should be increased. As the studies suggested that probiotics help reduce gestational diabetes with no reported side effects, they should be used along with other maternity medications.

Conclusion:

This study concluded that the usage of probiotics decreases gestational diabetes in high-risk pre-diabetic pregnant women.

Conflict of interest:

No conflict of interest was reported in this study.

Funding source:

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Permission:

It was taken from the ethical review committee of the institute

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