Iran Red Crescent Med J. 2018 July; 20(7):e60675. doi: 10.5812/ircmj.60675.

Published online 2018 May 5. **Research Article**

Effects of Garlic Pill on Blood Glucose Level in Borderline Gestational Diabetes Mellitus: A Triple Blind, Randomized Clinical Trial

Farnaz Faroughi,[1] Sakineh Mohammad-Alizadeh Charandabi,[2] Yousef Javadzadeh,[3] and Mojgan Mirghafourvand[1,*]

[1]Nursing and Midwifery Faculty, Tabriz University of Medical Sciences, Iran
[2]Social Determinates of Health Research Center, Nursing and Midwifery Faculty, Tabriz University of Medical Sciences, Iran
[3]Medical Philosophy and History Research Center, Department of Traditional Pharmacy, Faculty of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[*]*Corresponding author*: Mojgan Mirghafourvand, Associate Professor of Midwifery Group, Midwifery Department, Tabriz University of Medical Sciences, Tabriz, Iran. Tel: +98-9143206121, Fax: +98-4134796969, E-mail:mirghafourvandm@tbzmed.ac.ir

Received 2017 August 21; **Revised** 2017 October 09; **Accepted** 2017 November 18.

Abstract

Background: Women with borderline gestational diabetes mellitus (BGDM) have a higher risk of complications in comparison with normal women.
Objectives: The aim of this study was to determine the effects of garlic pill on fasting blood sugar (FBS) and relapse of prediabetes symptoms (primary outcomes), as well as blood pressure, neonatal anthropometric indices, and mode of delivery (secondary outcomes) in prediabetic pregnant women.
Methods: This triple-blind, randomized clinical trial was conducted on 49 women with prediabetes at 24 to 28 weeks of gestation in Tabriz, Iran, during 2015 - 16. The participants were assigned to the intervention (n, 26) and control (n, 23) groups using block randomization. The intervention group received a 400-mg garlic pill per day, while the control group received a placebo pill per day for eight weeks. Four and eight weeks following the intervention, FBS and blood pressure were measured. The newborns' anthropometric indices and mode of delivery were also recorded after delivery.
Results: The mean FBS level in the garlic group decreased from 106.6 (11.1) mg/dL before the intervention to 83.6 (6.3) mg/dL at four weeks after the intervention and 79.4 (6.1) mg/dL at eight weeks after the intervention (adjusted mean difference, -3.7). The garlic pill also led to a significant decrease in prediabetes symptoms at four weeks after the intervention ($P < 0.001$) and diastolic blood pressure at four and eight weeks after the intervention ($P = 0.041$), compared to the control group. No significant difference was observed between the groups in terms of systolic blood pressure at four and eight weeks after the intervention, anthropometric indices, or mode of delivery.
Conclusions: The results revealed that garlic pill could reduce FBS level, prediabetes symptoms, and diastolic blood pressure. However, further research with a larger sample size is required for more accurate results.

Keywords: Blood Sugar, Diabetes Mellitus, Garlic, Gestational, Prediabetic, Pregnancy

1. Background

Pregnancy is associated with various anatomic and physiological changes. A healthy pregnancy requires metabolic and hormonal adaptation, which involves the hypothalamus, as well as the pituitary, parathyroid, thyroid, and adrenal glands; this metabolic adaptation meets fetal needs during pregnancy (1). In addition, placental secretions, including progesterone, placental lactogen, corticotropin-releasing hormone, and growth hormone, along with maternal hormone changes, increase resistance to insulin, improve insulin excretion, and reduce the sensitivity of insulin target cells. Therefore, pregnancy is a diabetes-inducing stage, and gestational diabetes mellitus (GDM) is recognized as the most common metabolic disorder during this period. Overall, 18% of pregnant women around the world experience a degree of glucose tolerance at the end of the second trimester (1,2).

According to the world health organization (WHO), gestational prediabetes is a condition in which fasting blood sugar (FBS) exceeds the normal level, and blood glucose is higher than normal at two hours after administration of glucose (75 g), but lower than the limits for gestational diabetes (3). Research suggests that impaired carbohydrate tolerance in women with blood glucose higher than normal, but not high enough for diabetes, increases the risk of complications, compared to normal women.

In other words, complications associated with GDM are partly observed at different levels of carbohydrate impairment, such as prediabetes (4,5).

Borderline GDM (BGDM) is reportedly associated with a higher frequency of cesarean section, preterm birth, shoulder dystocia, macrosomia, birth damage, long-term postpartum hospitalization (with increased blood pressure), preeclampsia, neonatal hypoglycemia, hyperbilirubinemia, and stillbirth (4,6,7). Although risk factors for GDM are properly recognized, effects of BGDM on the health of mothers and infants are not clearly determined (6). The primary treatment for BGDM involves lifestyle changes including diet, physical activity, and weight loss. Drugs are also occasionally used for this purpose (3), while only long-term lifestyle changes can reduce the blood sugar level (8).

WHO reports that more than three-quarters of the population in developing countries use herbal medicine as a means of primary health care (9,10). Overall, herbal drugs and compounds are more favorable and cost-effective than chemical drugs (10). Garlic is a species, which belongs to the Amaryllidaceae family or genus Allium (11-13). It is widely known as a common spice and a popular treatment for different diseases and physiological disorders (14,15). It mainly consists of 0.1% - 0.36% of volatile compounds, and its medicinal properties are attributed to its sulfur-containing volatile constituents (16,17).

The aqueous and methanol extracts of garlic lead to a considerable decline in the blood sugar of rats with diabetes (18-20). The blood sugar-reducing effect of allicin from garlic is assumed to be related to an increase in liver metabolism, a reduction in insulin secretion of pancreatic cells, and an increase in the production of short-acting insulin (21). Garlic is used for medicinal purposes, and its therapeutic properties include cardiovascular improvement, improved immune system performance, decreased blood sugar and cholesterol levels, increased protection against microbial infections, and anticancer effects (22).

One-third of patients with diabetes use effective alternative medicines, such as garlic (23). According to WHO reports, garlic is used to treat blood sugar disorders in nonpregnant women and animals. Investigations indicate that garlic reduces the level of blood glucose in rats with diabetes (18,20,24) and rabbits (25). Although some studies (9,26-29) have been conducted on the reducing effects of garlic on blood sugar, no study has examined the effects of herbal drugs during pregnancy.

Considering the side effects of chemical drugs during pregnancy, lack of a rapid decline in blood sugar with lifestyle changes, increased incidence of pregnancy complications in diabetic women, absence of a safe medicine, and lack of research on this issue, we aimed to determine the effects of garlic pill on FBS and relapse of prediabetes symptoms at four and eight weeks after the intervention (primary outcomes), as well as blood pressure, neonatal anthropometric indices, and mode of delivery (secondary outcomes) in pregnant women with prediabetes.

2. Methods

2.1. Study Design and Sample

In this randomized controlled clinical trial, a triple-blind design was applied in which the participants, data collector, and data analyzer were not informed of the type of treatment. Women from different socioeconomic classes were selected during their visits to healthcare centers and Al-Zahra and Taleqani hospitals of Tabriz, Iran during 2015 - 2016. Al-Zahra hospital is a specialized referral center in Northwest of Iran, providing obstetrics, gynecology, oncology, neonatal, and perinatology services. It is equipped with 150 beds and six operating rooms. On the other hand, Taleqani hospital is a general 98-bed hospital, which provides various services, including general surgery, neonatal intensive care unit (NICU), delivery, neonatal, obstetrics, and gynecology services; it also admits patients with high-risk pregnancies. In general, the health centers of Tabriz are first-level public, governmental, or private referral centers.

The inclusion criteria were as follows in this study: 1, ultrasound data confirming singleton pregnancy and fetal health; 2, 24 to 28 weeks of pregnancy; 3, FBS level of 93 - 125 mg/dL; 4, normal results on a 2-hour oral glucose tolerance test with 75 g of glucose (< 180 mg/dL in 1 hour and < 153 mg/dL in 2 hours); 5, absence of maternal history of GDM or hypertension; 6, availability of phone number for follow-up; 7, lack of participation in similar studies; 8, availability of medical records at Al-Zahra hospital, Taleqani hospital, or health centers of Tabriz; 9, lack of chronic diseases (e.g., liver and digestive diseases); and 10, lack of allergy to garlic. On the other hand, the exclusion criteria were as follows: 1, history of infertility and use of assisted reproductive methods; 2, use of blood pressure medicines and anticoagulants such as aspirin; 3, the presence of allergy symptoms; 4, increased FBS level; and 5, use of drugs.

To determine the sample size based on the findings reported by Aalami-Harandi et al. (2014) (27), the sample size for each group was calculated to be 8 with m1 of 81.31 (FBS before the intervention), m2 of 75.13 (FBS after the intervention), SD1 of 1.91, SD2 of 2.04, two-sided alpha of 0.05, and power of 95%, using G*Power version 3.1.2. Considering the small sample size and lack of research on the second study objective (relapse of prediabetes at four and eight weeks after the intervention), the final sample size was assumed to be 49.

2.2. Sampling

Sampling was initiated after obtaining approval from the Ethics committee of the Tabriz University of Medical Sciences (5/4/1421) and registering the study on the Iranian registry of clinical trials (IRCT) website (IRCT201509193706N27). The research setting included Al-Zahra and Taleqani hospitals, along with general governmental health centers of Tabriz. Purposeful sampling method was applied, and the criteria for selecting eligible subjects included women at 24 - 28 weeks of gestation, FBS of 93 - 125 mg/dL, and normal results on the 2-hour oral glucose tolerance test with 75 g of glucose (< 180 mg/dL in 1 hour and < 153 mg/dL in 2 hours).

To select the participants, the researcher attended the study setting and visited all prediabetic women. After introducing herself, she explained the research objectives and methods to the participants. Then, the eligibility criteria were assessed, and a written informed consent was obtained from eligible women, who were willing to participate in the study. The sociodemographic questionnaire was also completed by the subjects.

2.3. Data Collection Tools

The participants were assessed prior to the intervention, as well as four and eight weeks after the intervention. Blood pressure was measured with a Diplomat mercury manometer (Germany). The proteinuria test was requested if blood pressure was not normal. Four and eight weeks after the intervention, the participants visited the laboratories of Taleqani and Al-Zahra hospitals at 8-10 a.m. to measure the FBS level (with an emphasis on 10-hour fasting). To measure FBS, 2 mL of blood was obtained from each participant, and FBS was measured in the serum or plasma, using a quantitative glucose diagnosis kit (GOD) through the photometric method. The participants were followed-up after childbirth, and neonatal anthropometric indices at birth, as well as the mode of delivery, were recorded on a checklist, based on the mothers' delivery records.

To determine the reliability of the experiments, two blood samples were randomly obtained from 5 pregnant women, and both samples were labeled differently in the laboratories of the mentioned health centers. The results were examined based on Pearson's correlation coefficient test, indicating a correlation of 0.99. The validity of the sociodemographic questionnaire was assessed using content validity, and the questionnaire content was evaluated by ten faculty members of Tabriz University of Medical Sciences. After receiving feedback and making the required corrections, the questionnaire was administered.

2.4. Randomization and Intervention

The participants were assigned to the intervention (garlic pill) and control (placebo) groups, using block randomization with four and six blocks (allocation ratio, 1:1). For concealed allocation, the drugs were placed inside a sealed envelope and numbered in sequence. The envelopes were prepared by a person, who was not involved in the sampling process or data analysis, and the data collector, data analyzer, and participants were blinded to the procedure.

The intervention and control groups received garlic and placebo pills (1 pill per day after a meal) for eight weeks, respectively. The garlic pill contained 400 mg of dry garlic powder (containing 1200 - 1800 mg of allicin and approximately 2 g of fresh garlic; Garrett Brand, Amin Pharmaceutical Company, Isfahan, Iran). The pills were purchased from a pharmacy. The placebo pill, with the same weight and appearance as the garlic pill, lacked the main medicine and contained starch; it was prepared by a pharmacist, using a combination of adjuvants in garlic pill.

2.5. Data Analysis

Data were analyzed by SPSS statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). At first, the normal distribution of data was determined with the Kolmogorov-Smirnov test; all data showed a normal distribution. Descriptive statistics (number, percentage, mean, and standard deviation) were used to describe the sociodemographic characteristics of the participants. Chi-square test, Chi-square test for trend, Fisher's exact test, and independent t-test were applied for comparing the sociodemographic characteristics between the groups.

The level of FBS, systolic blood pressure, and diastolic blood pressure were compared between the groups, using independent t-test before the intervention and repeated measures ANOVA at four and eight weeks after the intervention. To increase the study power, the baseline values of the outcomes were entered in the general linear model as covariates, along with variables which were significant in the groups, including education and occupation. In addition, before conducting multivariate analyses, assumptions of repeated measures ANOVA, including normality of residuals by time point and sphericity were studied.

Chi-square test was used to compare the frequency of relapse of prediabetes symptoms at four and eight weeks after the intervention and to compare mode of delivery between the groups. Independent t-test was also applied to compare neonatal anthropometric indicators. Analyses were carried out with the intention to treat, and in all stages, $\alpha < 0.05$ was considered statistically significant.

3. Results

Among 287 pregnant women at 24 - 28 weeks of gestation, who visited the aforementioned hospitals and health centers from October 24, 2015, to March 16, 2016, a total of 207 ineligible women were excluded from the study; also, 31 women were excluded due to the unwillingness to participate in the study. In total, 49 pregnant women participated in this study. However, three samples were eliminated at four weeks after the intervention (two subjects from the garlic group due to lack of access and one subject from the placebo group due to lack of cooperation), and two participants were excluded at eight weeks after the intervention (one subject from the garlic group and one subject from the placebo group due to lack of cooperation). Finally, 44 out of 49 participants remained in the study (Figure 1).

The mean age of the participants was 29.6 (SD, 5.2) years, and approximately 56% of women were nulliparous. Nearly 90% of participants had no history of abortion. Only one subject had a history of intrauterine fetal death, and one subject had a history of preterm birth. Moreover, about 70% of pregnancies were wanted, and almost 75% of women were housewives. There was no significant difference between the groups in terms of sociodemographic characteristics, except for women's education and occupation (Table 1).

The mean FBS level in the garlic group decreased from 106.6 (11.1) mg/dL before the intervention to 83.6 (6.3) mg/dL at four weeks after the intervention and 79.4 (6.1) mg/dL at eight weeks after the intervention. In the placebo group, the FBS level increased from 108.9 (11.4) mg/dL before the intervention to 106.1 (19.5) mg/dL at four weeks after the intervention and 101.3 (13.8) mg/dL at eight weeks after the intervention. Based on the independent t-test results, there was no significant difference between the groups before the intervention (P = 0.487).

According to the results of repeated measures ANOVA with adjustments for the baseline values and participants' education and occupation, the FBS level in the garlic group significantly decreased, compared to the placebo group after the intervention (adjusted mean difference, -22.0; 95% CI, -30.9 to -13.1). Regarding the FBS level after the intervention, there was no significant difference among women with different educational levels (F = 0.180; P = 0.947) or employed women and housewives (F = 0.128; P = 0.723). Also, the effects of time (F = 1.269; P = 0.268) and time × group (F = 2.343; P = 0.135) were not significant (Figure 1 and Table 2).

Among 26 women with prediabetes receiving garlic pills, only one woman was prediabetic at the end of the fourth week of intervention, while 25 patients demonstrated relapse of prediabetes symptoms. On the other hand, 18 participants from the placebo group remained prediabetic, and a significant difference was observed between the groups, according to the results of Chi-square test (P < 0.001). Moreover, at the end of the eighth week, symptoms of prediabetes relapsed in all pregnant women from the garlic group, whereas ten women from

Table 1. Sociodemographic Characteristics of the Groups[a]

Sociodemographic Characteristics	Placebo Group (N = 23)	Garlic Group (N = 26)	P Value[b]
Age, y			0.122[c]
20 - 29	9 (39.1)	16 (61.5)	
≥ 30	14 (60.9)	10 (38.5)	
Body mass index, kg/m^2			0.201[d]
18.5 - 24.9	5 (21.7)	12 (46.2)	
25 - 29.9	14 (60.9)	11 (42.3)	
> 30	4 (17.4)	3 (11.5)	
Level of education			< 0.001[d]
Secondary school and lower	7 (30.4)	10 (38.5)	
High school/diploma	1 (4.3)	14 (53.8)	
University	15 (65.2)	2 (7.7)	
Mother's occupation			0.006[e]
Housemaker	13 (65.5)	24 (92.3)	
Employed	10 (43.5)	2 (7.7)	
Parity			0.934[f]
Nulliparous	13 (56.5)	15 (57.7)	
Multiparous	10 (43.5)	11 (42.3)	
Number of deliveries			0.837[f]
0 - 1	20 (87)	21 (80.8)	
≥ 2	3 (13)	5 (19.2)	
Spouse's occupation			0.378[f]
Unemployed	0 (0.0)	2 (7.7)	
Employee	5 (21.7)	6 (23.1)	
Worker	4 (17.4)	4 (15.4)	
Shopkeeper	5 (21.7)	9 (34.6)	
Others[g]	9 (3.1)	5 (19.2)	
Spouse's educational level			0.303[d]
Secondary school and lower	5 (21.7)	7 (26.9)	
High school/diploma	9 (39.1)	14(53.8)	
University	9 (39.1)	5)19.2)	
Family income			0.912[d]
Adequate	11 (47.8)	13 (50.0)	
Quite adequate	10 (43.5)	10 (38.5)	
Inadequate	2 (8.7)	3 (11.5)	
Housing status			0.442[f]
House ownership	17 (73.9)	15 (57.7)	
Rental	4 (17.4)	6 (23.1)	
Parents' home	2 (8.7)	5 (19.2)	

[a] Data in the Table represent No. (%).
[b] P < 0.05 was considered significant.
[c] One-way ANOVA.
[d] Chi-square test for trend.
[e] Fisher's exact test.
[f] Chi-square test.
[g] Without a shop.

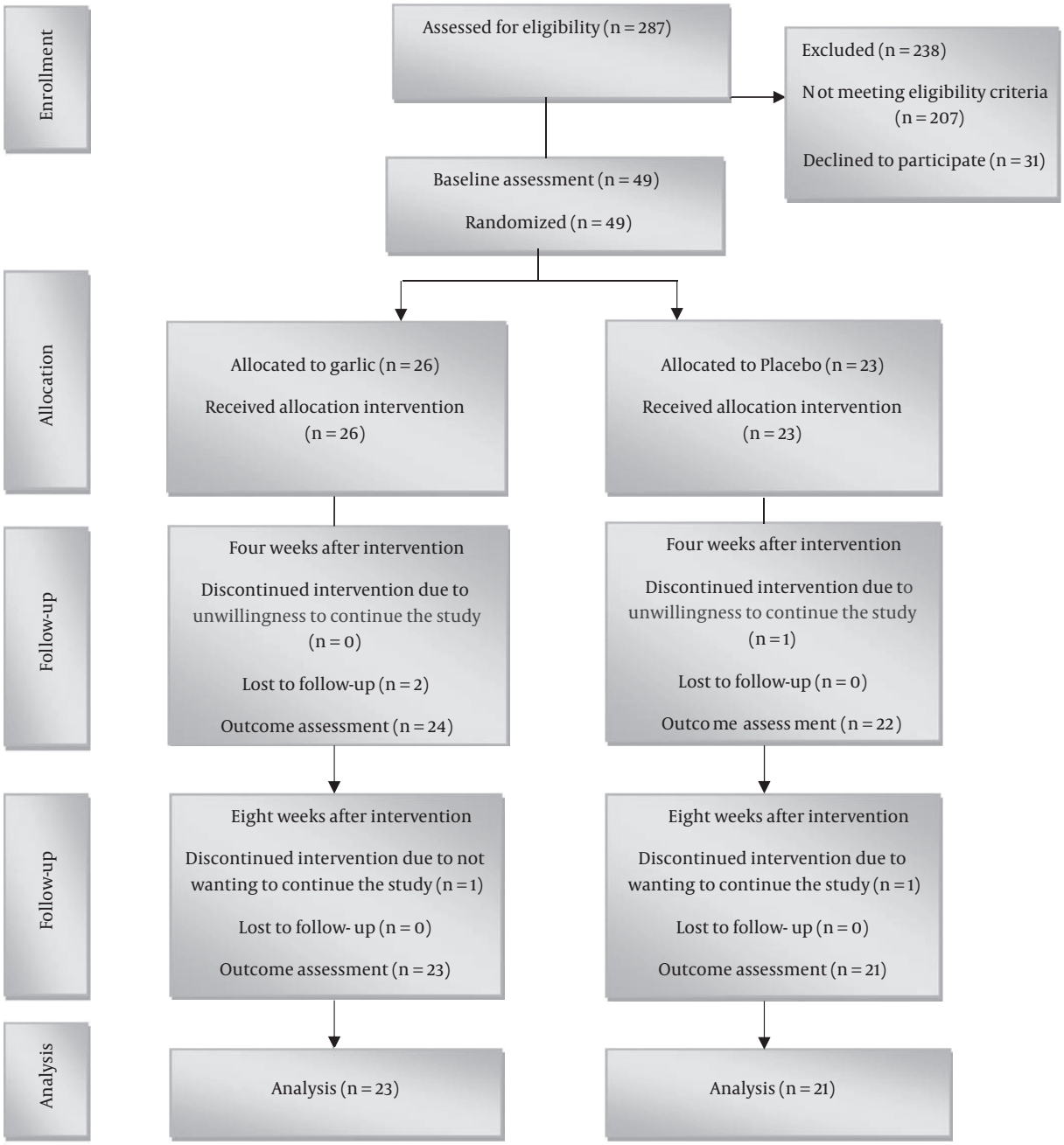

Figure 1. The study flowchart

the placebo group remained prediabetic, based on the FBS levels (Table 3).

The average systolic blood pressure in the garlic group changed from 112.3 (8.8) before the intervention to 107.2 (7.2) at four weeks after the intervention and 109.3 (8.5) at eight weeks after the intervention. In the placebo group, systolic blood pressure changed from 110.4 (10.6) before the intervention to 111.1 (9.5) at four weeks after the intervention and 110.5 (9.2) at eight weeks after the intervention. Based on the results of independent t-test, there was no significant difference between the groups before the intervention (P = 0.505).

Table 2. The Comparison of Systolic and Diastolic Blood Pressure and Fasting Blood Sugar (FBS) Before the Intervention and four and eight Weeks After the Intervention[a,b]

Groups	Garlic (N = 55)	Placebo (N = 57)	Comparison of Garlic and Placebo Groups, AMD (95% CI)	P Value[c]
FBS				
Baseline	106.6 (11.1)	108.9 (11.4)	-3.7 (-7.3 to -0.3)	0.487
After four weeks	83.6 (6.3)	106.1 (19.5)	-22.0 (-30.9 to -13.1)	0.001>
After eight weeks	79.4 (6.1)	101.3 (13.8)		
Systolic blood pressure				
Baseline	112.3 (8.8)	110.4 (10.6)	1.8 (-3.7 to 7.4)	0.505
After four weeks	107.2 (7.2)	111.1 (9.5)	-4.6 (-10.9 to 1.7)	0.149
After eight weeks	109.3 (8.5)	110.5 (9.2)		
Diastolic blood pressure				
Baseline	68.5 (6.9)	68.4 (8.7)	0.17 (-4.3 to 4.6)	0.938
After four weeks	64.3 (6.6)	66.5 (6.8)	-3.1 (-7.5 to 1.3)	0.162
After eight weeks	64.5 (5.9)	68.6 (7.9)		

Abbreviation: AMD (95% CI), Adjusted Mean Difference (95% CI)
[a] For comparison of groups before the intervention, independent t-test was applied, while after the intervention, repeated measures ANOVA with adjustments for baseline values was performed (variables of education and occupation were considered).
[b] Values are expressed as mean (SD).
[c] $P < 0.05$ was considered significant.

Table 3. The Frequency of Prediabetes Relapse and Mode of Delivery in the Groups at four and eight Weeks After the Intervention[a]

Outcomes	Garlic (N = 26)	Placebo (N = 23)	P Value[b]
Prediabetes before the intervention	26 (100)	23 (100)	-
Prediabetes after four weeks	1 (3.8)	18 (78.3)	< 0.001
Prediabetes after eight weeks	0	10 (43.5)	0.075
Mode of delivery			0.151
Caesarean section	11 (50)	15 (71.4)	
Natural vaginal delivery	11 (50)	6 (28.6)	

[a] Values are expressed as No. (%).
[b] P value based on Chi-square test ($P < 0.05$ was considered significant).

According to repeated measures ANOVA with adjustments for the baseline values and participants' education and occupation, systolic blood pressure in the garlic group did not significantly decrease, compared to the placebo group after the intervention (-3.9; -8.2 to -0.4; P = 0.076). In terms of the average systolic blood pressure after the intervention, there was no significant difference among women with different educational levels (F = 1.099; P = 0.372) or employed women and housemakers (F = 0.025; P = 0.875). Also, the effects of time (F = 0.001; P = 0.972) and time × group (F = 3.550; P = 0.068) were insignificant (Table 2).

The average diastolic blood pressure in the garlic group changed from 68.5 (6.9) before the intervention to 64.3 (6.6) at four weeks after the intervention and 64.5 (5.9) at eight weeks after the intervention. In the placebo group, diastolic blood pressure decreased from 68.3 (8.7) before the intervention to 66.9 (6.8) at four weeks after the intervention and 68.6 (7.9) at eight weeks after the intervention. Based on the independent t-test, there was no significant difference between the groups before the intervention (P = 0.938).

On the other hand, based on the repeated measures ANOVA with adjustments for the baseline values and participants' education and occupation, diastolic blood pressure decreased in the garlic group, compared to the placebo group following the intervention (-3.1; -7.5 to 1.3; P = 0.162); however, there was no significant difference between the groups. In terms of the average diastolic blood pressure after the intervention, there was no significant difference among women with different educational levels (F = 0.974; P = 0.434) or employed women and housewives (F = 0.011; P = 0.919). Also, the effects of time (F = 2.250; P = 0.143) and time × group (F = 0.423; P = 0.520) were not significant (Table 2).

In both groups, gestational age was 37 weeks or higher at birth. In addition, mode of delivery was the cesarean section in 50% of participants from the garlic group and 71.4% of participants from the placebo group; however, no significant difference was observed between the groups (P = 0.151; Table 3). Moreover, no significant difference was observed between the garlic and placebo groups in terms of anthropometric indicators (P > 0.05). The average weight, height, and head circumference in the garlic group were 3171.52, 50.65, and 33.08, respectively. The corresponding values were 3107.5 (457.6), 49.8 (3.6), and 33.3 (2.7), respectively in the placebo group (Table 4).

Four weeks after the intervention, 22 (84.6%) women from the garlic group and 20 (86.9%) women from the placebo group were highly satisfied with the intervention. In the eighth week of the intervention, 22 (84.6%) participants from the garlic group and 15 (65.2%) participants from the placebo group were also highly satisfied. There was a significant difference in the level of satisfaction between the groups, based on the results of the Mann-Whitney U test (P < 0.001). Four weeks after the intervention, one participant from the placebo group experienced vertigo, while eight weeks after the intervention, one subject from the garlic group complained of headaches.

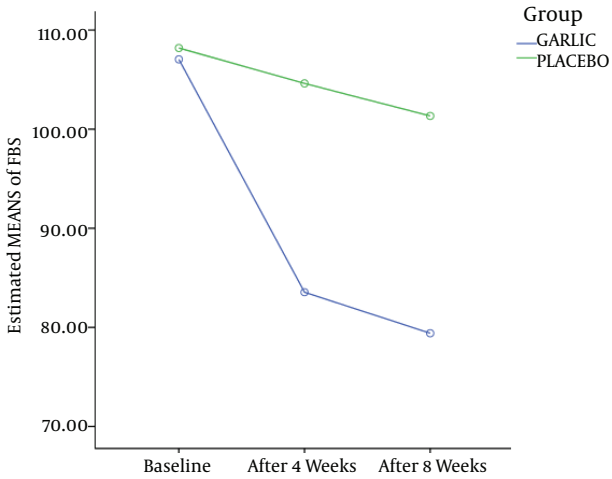

Figure 2. The Trend of changes in the mean fasting blood sugar (FBS) in mothers with borderline gestational diabetes mellitus (BGDM) at two follow-up points

4. Discussion

This trial was designed to assess the effects of garlic pill on pregnant women with prediabetes. Previous investigations have revealed the adverse effects of gestational prediabetes on the outcomes of pregnancy and childbirth (4,6,7). In this study, the average FBS level significantly decreased in the group receiving garlic pills (400 mg; one pill per day after a meal), compared to the placebo group after four and eight weeks of the intervention. Moreover, garlic pills led to the significant relapse of prediabetes symptoms at four weeks after the intervention, as well as diastolic blood pressure at four and eight weeks after the intervention, compared to the control group. However, no significant difference was observed between the groups in terms of systolic blood pressure, neonatal anthropometric indices, or mode of delivery.

With its active sulfurous compounds, such as allicin, cysteine sulfoxide, allyl propyl disulfide, and S-allyl, garlic reduces the level of blood sugar by inhibiting liver-induced activation of insulin, increasing insulin secretion from pancreatic beta cells or further insulin isolation from bonded forms, and increasing insulin sensitivity of cells. The allicin content of garlic also inhibits the activity of angiotensin II, which is responsible for the increase in blood pressure. Garlic also contains a substance, known as polysulfide, which is transformed into hydrogen sulfide gas by red blood cells, causing vasodilatation and consequently reduced blood pressure (11-13).

The findings of the present research are in line with previous human and animal studies. In animal studies, garlic reduced the blood glucose level in rats with diabetes (18,20,24) and rabbits (25). In this regard, Kumar et al. (9) studied 60 patients with type II diabetes and reported that simultaneous intake of 500 mg of metformin (twice or 3 times a day) and 250 g of garlic (twice a day) for twelve weeks reduced the FBS level. However, since metformin has side effects, such as preterm birth and reduced maternal weight gain (30), and is associated with financial limitations and complications (hypoglycemia, overweight, digestive disorders, and hepatotoxicity) (21), it is recommended to replace metformin with garlic pill for prediabetes to prevent GDM.

Ebadi et al. (26) also studied 60 patients with type II diabetes and found that daily consumption of six 400-mg garlic pills for 3 months significantly reduced FBS and glycosylated hemoglobin, compared to the control group. In this study, low doses of garlic were used due to pregnancy and lack of high blood sugar in women with prediabetes. Nonetheless, the results of the present study do not comply with the findings reported by Parastouei et al. (31), who studied 50 patients with type II diabetes and hyperlipidemia. They reported that daily consumption of three 300-mg garlic powder pills for six weeks was not effective in reducing FBS and diastolic blood pressure. One of the possible reasons for the contradictions between the present study and the mentioned research may be the differences among the participants and research periods (six

Table 4. The Comparison of Neonatal Anthropometric Indices Between the Garlic and Placebo Groups[a]

Outcomes	Garlic Group	Placebo Group	Group Comparisons	
			MD (95% CI)[b]	P Value[c]
Head circumference	32.9 (3.1)	33.3 (2.7)	-0.4 (-2.2 to 1.4)	0.661
Weight	3165.6 (445.4)	3107.5 (457.6)	58.1 (-219.9 to 336.2)	0.675
Height	50.6 (2.4)	49.8 (3.6)	0.87 (-1.02 to 2.7)	0.359

[a]Values are expressed as mean (SD).
[b]Mean difference (95% CI) based on independent t-test.
[c]$P < 0.05$ was considered significant.

weeks versus eight weeks). In addition, the patients in the mentioned study had cholesterol levels above 220 mg/dL, and therefore, the existing contradiction can be explained since fat increases insulin resistance (32).

Additionally, Aalami-Harandi et al. (27) studied the effects of daily intake of 400-mg garlic pills for nine weeks on 44 pregnant women prone to preeclampsia. They found that garlic reduced the high sensitivity of C-reactive proteins, increased plasma glutamine, reduced FBS, and increased sensitivity to insulin. In this study, garlic pills only reduced diastolic blood pressure and FBS and did not affect systolic blood pressure. On the other hand, Nahid Akbari (33) and Reza Soltani (34) studied the effects of 800-mg garlic pills on blood pressure in 100 pregnant women prone to preeclampsia for 6 - 8 weeks and concluded that garlic pill could reduce systolic and diastolic blood pressure. The results of the present study suggest a decline in diastolic blood pressure and are in line with the mentioned research.

Furthermore, Zamani Nour et al. (28) studied the effects of daily intake of garlic for three months on 25 patients with type II diabetes. They found that garlic reduces the level of FBS. Allicin in garlic reduces blood glucose due to increased liver metabolism, increased insulin release from pancreatic cells, and short-acting insulin production. In this regard, Afkhami-Ardekani et al. (29) studied the effects of daily intake of 900-mg garlic pills for four weeks on 45 patients with type II diabetes and hyperlipidemia. They found that garlic could reduce the levels of FBS, cholesterol, and serum lipids. In this study, garlic significantly decreased fasting blood glucose and serum lipids. Therefore, the researchers concluded that this pill could be helpful in the treatment of diabetic and hyperlipidemic patients. The results of the mentioned studies are consistent with the findings of the present research regarding the reduction in blood glucose level.

The strengths of this study include consideration of all randomized clinical trial principles, such as random allocation and allocation concealment to prevent bias. The present study is the first study to assess the effects of garlic on pregnant women with prediabetes. Previous studies have assessed nonpregnant women, pregnant women prone to preeclampsia, and patients with diabetes. The findings revealed that garlic pill reduces FBS and diastolic blood pressure and results in the relapse of prediabetes symptoms. Therefore, by prescribing garlic (as an herbal medicine) for pregnant women with prediabetes, it may be possible to prevent progression of gestational diabetes and its complications.

One of the limitations of this study is the small sample size and short follow-up. Therefore, if follow-up continues for more than eight weeks in future studies, parameters including blood pressure will probably change. Moreover, factors such as environmental stress and lifestyle were not controllable. Therefore, it is recommended to study the effects of garlic pills on pregnant women prone to increased blood sugar in the first months of pregnancy, based on body mass index to prevent hyperglycemia through long-term follow-ups. Since herbal medicines can considerably influence diabetes mellitus, it is recommended to examine the effects of garlic pill on the rapid improvement of women with prediabetes, receiving metformin and insulin, by measuring hemoglobin A1c before and after the intervention.

4.1. Conclusion

The results revealed that consumption of garlic pill could reduce FBS and diastolic blood pressure and also result in the relapse of prediabetes symptoms in pregnant women. However, further research with a larger sample size is required for more accurate results.

Acknowledgments

This paper was extracted from a Master's thesis, approved and funded by the research deputy of Tabriz University of Medical Sciences. The authors hereby appreciate the cooperation and assistance of Dr. Fatemeh Abas Alizadeh, Dr. Dowlatkhah, and Roqayeh Kazemi, as well as the personnel of Tabriz healthcare centers, Al-Zahrah Hospital,

and Taleqani Hospital, who sincerely collaborated with us in the sampling procedures.

Footnote

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Bangale D. High risk cases in obstetrics pregnancy. *Jaypee Brothers Medical Publishers*. 2014:428.
2. Briana DD, Malamitsi-Puchner A. Reviews: adipocytokines in normal and complicated pregnancies. *Reprod Sci*. 2009;**16**(10):921–37. doi: 10.1177/1933719109336614. [PubMed: 19474287].
3. World Health Organization . *Diabetes programme.Defining intermediate states of hyperglycemia*. 2017. Available from:http://www.who.int/diabetes/action_online/basics/en/index2.html.
4. Larijani B, Azizi F, Bastan-Hagh M, Pajuhi M, Hosein-Nejad A. The prevalence of gestational diabetes mellitus in young women. *J Endocrinol MetabJ Endocrinol Metab*. 2002;**4**(1):23–9. Persian.
5. Jensen DM, Damm P, Sorensen B, Molsted-Pedersen L, Westergaard JG, Klebe J, et al. Clinical impact of mild carbohydrate intolerance in pregnancy: a study of 2904 nondiabetic Danish women with risk factors for gestational diabetes mellitus. *Am J Obstet Gynecol*. 2001;**185**(2):413–9. doi: 10.1067/mob.2001.115864. [PubMed: 11518901].
6. Ju H, Rumbold AR, Willson KJ, Crowther CA. Borderline gestational diabetes mellitus and pregnancy outcomes. *BMC Pregnancy Childbirth*. 2008;**8**:31. doi: 10.1186/1471-2393-8-31. [PubMed: 18664297].
7. Yogev Y, Xenakis EM, Langer O. The association between preeclampsia and the severity of gestational diabetes: the impact of glycemic control. *Am J Obstet Gynecol*. 2004;**191**(5):1655–60. doi: 10.1016/j.ajog.2004.03.074. [PubMed: 15547538].
8. Bain E, Crane M, Tieu J, Han S, Crowther CA, Middleton P. Diet and exercise interventions for preventing gestational diabetes mellitus. *Cochrane Database Syst Rev*. 2015;(4). CD010443. doi: 10.1002/14651858.CD010443.pub2. [PubMed: 25864059].
9. Kumar R, Chhatwal S, Arora S, Sharma S, Singh J, Singh N, et al. Antihyperglycemic, antihyperlipidemic, anti-inflammatory and adenosine deaminase- lowering effects of garlic in patients with type 2 diabetes mellitus with obesity. *Diabetes Metab Syndr Obes*. 2013;**6**:49–56. doi: 10.2147/DMSO.S38888. [PubMed: 23378779].
10. Luqman S, Rizvi SI, Beer AM, Khare SK, Atukeren P. Efficacy of herbal drugs in human diseases and disorders. *Evid Based Complement Alternat Med*. 2014;**2014**:273676. doi: 10.1155/2014/273676. [PubMed: 25045388].
11. Block E. *Garlic and Other Alliums. The Lore and the Science Royal Society of Chemistry*. 2010.
12. Eja ME, Asikong BE, Abriba C, Arikpo GE, Anwan EE, Enyi-Idoh KH. A comparative assessment of the antimicrobial effects of garlic (Allium sativum) and antibiotics on diarrheagenic organisms. *Southeast Asian J Trop Med Public Health*. 2007;**38**(2):343–8. [PubMed: 17539285].
13. Singh TU, Kumar D, Tandan SK, Mishra SK. Inhibitory effect of essential oils of Allium sativum and Piper longum on spontaneous muscular activity of liver fluke, Fasciola gigantica. *Exp Parasitol*. 2009;**123**(4):302–8. doi: 10.1016/j.exppara.2009.08.002. [PubMed: 19679128].
14. Singh V, Singh D. Pharmacological Effects of Garlic (Allium sativum L.). *ARBS Annu Rev Biomed Sci*. 2008;**10**:6–26.
15. Kathi K. Garlic (Allium sativum). *Longwood Herbal Task Force*. 2000.
16. Qudry J. *A text book of pharmacognosy*. 15th ed. India: B.S. Shah Prakashan; 2009. p. 15–156.
17. Roman-Ramos R, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. *J Ethnopharmacol*. 1995;**48**(1):25–32. doi: 10.1016/0378-8741(95)01279-M. [PubMed: 8569244].
18. Jelodar GA, Maleki M, Motadayen MH, Sirus S. Effect of fenugreek, onion and garlic on blood glucose and histopathology of pancreas of alloxan-induced diabetic rats. *Indian J Med Sci*. 2005;**59**(2):64–9. doi: 10.4103/0019-5359.13905. [PubMed: 15738612].
19. Jalal R, Bagheri SM, Moghimi A, Rasuli MB. Hypoglycemic effect of aqueous shallot and garlic extracts in rats with fructose-induced insulin resistance. *J Clin Biochem Nutr*. 2007;**41**(3):218–23. doi: 10.3164/jcbn.2007031. [PubMed: 18299719].
20. Mostofa M, Choudhury ME, Hossain MA, Islam MZ, Islam MS, Sumon MH. Antidiabetic effects of Catharanthusroseus, Azadirachtaindica, Allium sativum and glimepride in experimentally diabetic induced rat. *Bangladesh J Vet Med*. 2008;**5**(1). doi: 10.3329/bjvm.v5i1.1324.
21. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. *J Clin Biochem Nutr*. 2007;**40**(3):163–73. doi: 10.3164/jcbn.40.163. [PubMed: 18398493].
22. Ashraf R, Aamir K, Shaikh AR, Ahmed T. Effects of garlic on dyslipidemia in patients with type 2 diabetes mellitus. *J Ayub Med Coll Abbottabad*. 2005;**17**(3):60–4. [PubMed: 16320801].
23. Ryan EA, Pick ME, Marceau C. Use of alternative medicines in diabetes mellitus. *Diabet Med*. 2001;**18**(3):242–5. doi: 10.1046/j.1464-5491.2001.00450.x. [PubMed: 11318847].
24. Drobiova H, Thomson M, Al-Qattan K, Peltonen-Shalaby R, Al-Amin Z, Ali M. Garlic increases antioxidant levels in diabetic and hypertensive rats determined by a modified peroxidase method. *Evid Based Complement Alternat Med*. 2011;**2011**:703049. doi: 10.1093/ecam/nep011. [PubMed: 19233877].
25. Mahesar H, Bhutto M, Khand A, Narejo N. Garlic used as an alternative medicine to control diabetic mellitus in alloxan-induced male rabbits. *Pak J Physiol*. 2010;**6**(1):39–41.
26. Ebadi A, Rahimi E, Taghadosi M, Khorshidi A, Akbari H. Effect of garlic on blood glucose in type 2 diabetic patients. *Feyz*. 2007;**11**(1):20–5. Persian.
27. Aalami-Harandi R, Karamali M, Asemi Z. The favorable effects of garlic intake on metabolic profiles, hs-CRP, biomarkers of oxidative stress and pregnancy outcomes in pregnant women at risk for pre-eclampsia: randomized, double-blind, placebo-controlled trial. *J Matern Fetal Neonatal Med*. 2015;**28**(17):2020–7. doi: 10.3109/14767058.2014.977248. [PubMed: 25316559].
28. Zamani Nour N, Tahbaz F, Taleban F, Alavi Majd H, Neyestani T. Effects of garlic ingestion with breakfast on postprandial serum glucose and insulin in type 2 diabetic patients. *Iran J Nutr Sci Food Technol*. 2007;**1**(3):39–44. Persian.
29. Afkhami -Ardekani M, Kamali-Ardakani A. Study of the effect of garlic on serum lipids and blood glucose levels in type 2 diabetic patients. *J Shahid Sadoughi Univ Med Sci*. 2006;**13**(1):8–11. Persian.
30. Hunt KF, Whitelaw BC, Gayle C. Gestational diabetes. *Obstet Gynaecol Reprod Med*. 2014;**24**(8):238–44. doi: 10.1016/j.ogrm.2014.05.005.
31. Parastouei K, Ravanshad S, Mostafavi H, Sutude-Maram E. Effect of pills "garlic" on glucose, plasma lipids and blood pressure in type II diabetic patients with hyperlipidemia. *Journal of Medicinal Plant*. 2006;**1**(17):48–54. Persian.
32. Carey DG, Jenkins AB, Campbell LV, Freund J, Chisholm DJ. Abdominal fat and insulin resistance in normal and overweight women: Direct measurements reveal a strong relationship in subjects at both low and high risk of NIDDM. *Diabetes*. 1996;**45**(5):633–8. [PubMed: 8621015].
33. Akbari N. Effect of garlic on prevention of pre-eclampsia in women at high risk. *J Sabzevar Univ Med Sci*. 2001;**8**(2):71–8. Persian.
34. Reza Soltani P. Effect of garlic on plasma lipids and platelet aggregation in nulliparous pregnant women with a high risk of preeclampsia. *J Med Council Islamic Republic Iran*. 2005;**23**(3):250–8.