

Effect of 2-week bedtime ingestion of apple cider vinegar on the blood glucose concentration (fasting blood sugar and second hour blood sugar) of gravidas with gestational diabetes mellitus in a tertiary hospital*

BY MYRA G. CASIPLE-SOLAS, MD AND MARIA DOLORES A. MERCADO, MD, FPOGS
Department of Obstetrics and Gynecology, Angeles University Foundation Medical Center

ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) is a common condition that complicates a substantial number of pregnancies. Currently, the first line management for patients with GDM is dietary modification and exercise. Recent evidence suggest that there may be a complimentary hypoglycemic effect of substances such as vinegar.

Objectives: This study is a randomized, crossover trial, aiming to determine the effect of 2-week bedtime ingestion of apple cider vinegar (ACV) on the blood glucose concentration of gravidas diagnosed with GDM in a tertiary hospital. Specifically, it aims to describe the patients' general profile, to determine the effect of ACV on the 75 grams OGTT levels of the subjects, to correlate the change in blood glucose levels with ingestion of the same amount of ACV with the patient's BMI, and to determine the acceptability of ACV ingestion in pregnant patients.

Methods: There were 32 patients included in the study. Upon diagnosis of GDM, subjects were randomized into two groups. Group A had a sequence of Medical Nutrition Therapy (MNT) for 2 weeks followed by MNT plus ingestion of 2 tablespoons of ACV diluted in a cup of water for another 2 weeks. Group B had the reverse sequence. A 75g OGTT was taken on Day 0, Day 14, and Day 28 of treatment, in which the values were compared. The data were analyzed using SPSS 16.0.

Results: Results showed that there is a marginally significant increase in the fasting blood sugar (FBS) and 2nd hour blood sugar at the moment when ACV was withdrawn. A greater reduction in the blood sugar level was noted in patients with higher BMI during the period when patients were given the ACV. The Likert scale response was also done showing that ACV is acceptable, affordable and well-tolerated among pregnant patients.

Keywords: Gestational Diabetes Mellitus, apple cider vinegar, pregnancy, hypoglycemic effect

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is undeniably a common condition that complicates a substantial number of pregnancies.¹ Worldwide, they affect approximately 1-14% of all pregnancies. In the Philippines, 5.1% of women surveyed had type 2 diabetes mellitus or GDM.³ Treating GDM is important because it reduces serious perinatal morbidity and at the same time, it may improve the woman's health status and quality of life.⁶

Currently, the first line management for patients with GDM is dietary modification and exercise.⁴ Based on recent guidelines, Medical Nutrition Therapy (MNT) should be an integral part of GDM management, which may be administered as sole management approach or in combination with pharmacologic treatment to maintain normal glycemic control. It consists of an assessment of food intake, physical activity and medication history and intake, as well as weight status during and after pregnancy.³

Recent evidence suggests that there may be a complementary hypoglycemic effect of substances such as vinegar.^{2,4} There were several studies which identified the proposed physiological mechanisms of action of vinegar which include decreased gastric motility, increasing satiety, inhibited disaccharides metabolism, and increased hepatic and skeletal muscular glycogen

*First Place, Central Luzon Philippine Obstetrical and Gynecological Society (Foundation), Inc. (POGS) Research Contest, July 2017

storage.^{4,14} These are the properties that are in fact being harnessed by oral hypoglycemic pharmaceuticals.⁴

Apple cider vinegar (ACV) is an example. It is made from fresh apple juices that underwent fermentation to alcohol and oxidation to mainly acetic acid (5%).⁵ It also contains citric, formic, lactic, malic, succinic acids.⁵ It has a pH value of 2.8-3.0, with caloric value of 65 kilocalories, 16g carbohydrates, < 0.5g protein and 0g fat in every 100 ml.¹⁷ Compared to other vinegars in the market, which are mostly used in cooking and cleaning, ACV has more tolerable taste and literatures support its superiority in providing wide-range health benefits as anti-microbial, anti-fungal, anti-tumor, antiseptic, antidiabetic and breakthrough in managing gall bladder and kidney stones, and heart burn.^{2,11}

In veterinary practice, it has been used as part of the rations even in pregnant, lactating and laying animals like cows and rabbits for the treatment of external and internal ailments, and has shown favorable effects.¹⁵ It has no reported teratogenic effects in animal subjects even if they were given in large doses.^{7,8}

Vinegar is undeniably part of the daily Filipino diet, whether for pregnant or not. The United States Food and Drug Administration affirmed that acetic acid, the main ingredient of vinegar, is generally recognized as safe as a multipurpose food additive.⁸ It is also not included among the list of foods to avoid during pregnancy.⁹

Apple cider vinegar is readily available and affordable and has proven hypoglycemic and other health benefits among non-pregnant animal and human subjects.^{2,4,11,13} Hence, it offers a great potential to be evaluated further as to its complementary hypoglycemic effect in gravidas with GDM.^{2,4} To this date, there is still a paucity of data exploring these possibilities with pregnant subjects. Hence, the reason for the conduct of this study.

OBJECTIVES

A. General Objective

To determine the effect of 2-week bedtime ingestion of Apple Cider Vinegar on the blood glucose concentration of gravidas with Gestational Diabetes Mellitus in a tertiary hospital.

B. Specific Objectives

1. To describe the patients' general profile as to age, obstetric score and age of gestation upon enrollment to the study, and Body Mass Index (BMI)
2. To determine the effect of apple cider vinegar ingestion on the 75 grams OGTT levels of patients with gestational diabetes mellitus

3. To correlate the change in blood glucose levels after bedtime ingestion of the same amount of apple cider vinegar with the patient's BMI.
4. To determine the acceptability of apple cider vinegar ingestion in pregnant patients as to its taste, ease of use at bedtime, affordability, and occurrence of acid reflux or any other adverse reactions.

MATERIALS AND METHODS

Study Design: Randomized, Cross-over trial

Study Population: The study population consisted of 32 pregnant women, of any age and obstetric score, diagnosed with Gestational Diabetes Mellitus at any age of gestation, in a tertiary hospital, seen at the outpatient department from September to December 2016.

Inclusion Criteria: All pregnant women diagnosed with Gestational diabetes Mellitus during the 75g OGTT testing regardless of the baseline BMI. (see Figure 1)

Exclusion Criteria:

- Women with preexisting Type I and Type 2 Diabetes Mellitus who became pregnant, because they may already be on oral hypoglycemic agents therapy or on Insulin, which may affect the result of the study
- Patients diagnosed with GDM or Overt DM on the initial FBS, RBS, or HbA1C testing. (see Figure 1). This is to ensure uniformity of the glucose determination tool during the study, which is the 75g OGTT.
- Known allergy to Apple Cider Vinegar
- Patients who after started with 2-week diabetic diet had >50% increase in the blood sugar values will be considered drop out in the study because they might already need insulin therapy.

Sample size: Sample size could not be computed a priori due to the lack of needed inputs from existing literature. Hence, power analysis was done in retrospect. The actual sample size of 16 per treatment group achieved 79% power for detecting a difference at 5% significance level given the mean change of 2.50 ± 13.83 mg/dl in the group which had diet only for the first 2 weeks versus the mean change of -15.35 ± 21.84 in the group, which had diet with ACV for the first 2 weeks.

Study Procedure: As part of the standard prenatal checkup, all pregnant patients seen at the outpatient underwent the universal screening using the protocol for

the evaluation of diabetes in pregnant Filipino women based on Philippine Obstetrical and Gynecological Society Clinical Practice Guidelines (POGS CPG) Consensus on Diabetes Mellitus in Pregnancy, 2011 (Figure 1).³ Once the patient was diagnosed to have GDM during the 75g OGTT testing, she was asked by the researcher to sign an informed consent to be part of the study (Figure 1). Once consent was secured, patient profile as to age, obstetric score, age of gestation upon enrollment to the study, and current BMI were noted. Patients were referred to the hospital's dietary services for dietary advice and formulation of their Medical Nutrition Therapy (MNT).

The patients were then randomized into 2 groups through sealed envelopes. Group A had the sequence of 2-week individualized MNT alone followed by the 2-week MNT plus bedtime ingestion of 2 tablespoons (30 ml) of ACV diluted in 1 cup (237ml) of water to make a total volume of 267ml.^{2,17} A 450 ml commercially available filtered ACV was distributed to the patients. Group B had the reverse sequence. The 2-week period for each treatment was adapted as it is the recommended time to observe if diabetic diet is effective in reducing the blood sugar.^{3,21} The test diet followed each other in sequence without a break. No washout period was employed in between since the test diet periods were enough so that the endpoint measurements were not influenced by the previous diet.¹⁰

After randomization, the patient's baseline 75g OGTT levels was noted. After 2 weeks of either the individualized MNT alone or MNT plus ACV ingestion, a repeat 75g OGTT was done after adequate fasting. After another 2 weeks of either the individualized MNT alone or MNT plus ACV ingestion, final 75g OGTT determination was done and values were tabulated.

The 75g OGTT, which includes the fasting blood sugar (FBS) and the 2h blood sugar (2hBS), were chosen as the blood glucose determination tool because these tests measured different alterations, which are useful in combination. The FBS component was reflective of defective insulin secretion while the 2hBS reflected insulin resistance.¹²

After the final 75g OGTT determination, patients were asked to accomplish a researcher-constructed questions for the questionnaire, which were answerable by responses for a Likert scale.

Data Analysis: Statistical Analysis was performed using SPSS 16.0 with the level of significance set at P value <0.05. The paired t-test was used to analyze the blood sugar levels within groups and an independent t-test was used between groups. Pearson correlation was used to determine the correlation between the BMI and changes in blood sugar levels. Frequency and percent were also used

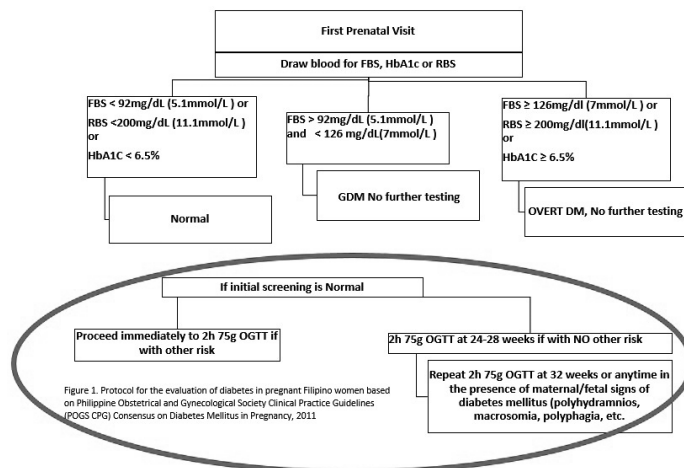


Figure 1. Protocol for the evaluation of diabetes in pregnant Filipino women based on Philippine Obstetrical and Gynecological Society Clinical Practice Guidelines (POGS CPG) Consensus on Diabetes Mellitus in Pregnancy, 2011

to analyze the responses in the Likert scale for evaluation of the acceptability of apple cider vinegar among pregnant patients.

Ethical Considerations: The research proposal was evaluated and approved by the Institutional Review Board. An informed consent were obtained from the participants prior to the conduct of the study. The purpose and conduct of the study, risks and inconveniences, possible benefits and compensation for the participant, provisions for injury, voluntariness and confidentiality were carefully discussed to the patients. A copy of the patients' information and informed consent were given to the subjects.

RESULTS

The study had 32 pregnant subjects diagnosed with Gestational Diabetes Mellitus (GDM). They were 21 to 42 years old with ages of gestation starting 7 weeks and 6 days to 32 weeks and 2 days upon enrollment to the study. Their body mass index (BMI) ranged from 19.4 to 30.3 kg/m² (Table 1).

Comparing the FBS results of both groups A and B, the baseline values were comparable. During the first 2 weeks in group A, where diabetic diet only was administered, the FBS result was reduced by 1.17mg/dl. However, in group B, where patients were given diabetic diet plus diluted apple cider vinegar, the FBS was reduced by a mean difference of 6.30 mg/dl, which is marginally significant (Table 2). On the last 2 weeks, the FBS in group A who was now given diabetic diet and Apple cider vinegar, had a greater mean difference of 2.60 mg/dl but was not statistically significant. Notice however, that in the last 2 weeks of treatment in group B, where apple cider was withdrawn,

the FBS increased by 3.98 mg/dl (Table 4).

In the 2nd hour blood sugar determination, the first 2 weeks for both groups A and B revealed results which are consistent with that of the trend of reduction in FBS results (see Table 3). On the last 2 weeks in group A where apple cider was added to the diabetic diet, there was a mean difference of 5.03 mg/dl. However, see that in group B, there was a statistically significant increase in the mean difference of the 2nd hour post prandial blood glucose by 15.35 mg/dl, signifying that once the ACV was

withdrawn and the age of gestation progressed, the blood sugar increased (see table 5). The result of this study was consistent with the study of White et al, wherein bedtime ingestion of vinegar after mealtime was employed leading to decrease morning FBS. This suggest that there could be an alternative mechanism independent of the ingestion of food.

All the subjects received the same amount of ACV amounting to 2 tablespoons (30 ml). The BMI upon enrollment to the study were also noted and correlated

Table 1. Demographic Information of GDM participants

	GROUP A n=16	Mean	GROUP B n=16	Mean	Total Number of Participants n=32	Mean
AGE						30.81
< 20 years	0	0	0	0	0	
20-29 years	5	24.4	5	23.6	10	
30-39 years	10	33.2	11	33.81	21	
40-49 years	1	42	0	0	1	
Gravidity						
Primigravid	2		9		12	
Multigravid	14		7		20	
Age of Gestation						
First Trimester	7		5		12	
Second Trimester	8		8		16	
Third Trimester	1		3		4	
BMI						20.44
< 18.5 kg/m ²	0	0	0	0	0	
≥ 18.5 to 24.99 kg/m ²	9	20.81	13	21.69	21	
≥ 25.0 to 29.99 kg/m ²	6	26.62	3	26.8	10	
>30 kg/m ²	1	30.3	0	0	1	

Table 2. Mean Difference in FBS in both groups from day 0 to day 14

	Mean Baseline FBS	Mean FBS after 2 weeks of diet only	p-value	Mean Difference in FBS
Group A (n = 16)	92.73	91.56	.58	1.17
	Mean Baseline FBS	Mean FBS after 2 weeks of diet + ACV	p-value	Mean Difference in FBS
Group B (n = 16)	95.21	88.90	.07	6.30
p-value	0.35	0.52		0.20

Table 3. Mean Difference in 2nd hour blood sugar from day 0 to day 14

	Mean Baseline 2H BS	Mean 2H BS after 2 weeks of diet only	p-value	Mean Difference in 2H PPBS
Group A (n = 16)	138.43	126.25	.13	12.18
	Mean Baseline 2H PPBS	Mean 2H PPBS after 2 weeks of diet + ACV	p-value	Mean Difference in 2H PPBS
Group B (n = 16)	137.84	124.26	.15	13.58
p-value	0.84	0.95		0.81

Table 4. Mean Difference in FBS in both groups from day 14 to day 28

	Mean FBS after 2 weeks of diet only	Mean FBS after 2 weeks of diet + ACV	p-value	Mean Difference in FBS
Group A (n = 16)	91.56	88.96	0.24	2.60
	Mean FBS after 2 weeks of diet + ACV	Mean FBS after 2 weeks of diet only	p-value	Mean Difference in FBS
Group B (n = 16)	88.90	92.88	0.21	-3.98
p-value	0.52	0.31		0.09

Table 5. Mean difference in 2nd hour post prandial blood sugar in both groups from day 14 to day 28

	Mean 2H PPBS after 2 weeks of diet only	Mean 2H PPBS after 2 weeks of diet + ACV	p-value	Mean Difference in 2H PPBS
Group A (n = 16)	126.25	121.22	0.48	5.03
	Mean 2H PPBS after 2 weeks of diet + ACV	Mean 2H PPBS after 2 weeks of diet only	p-value	Mean Difference in 2H PPBS
Group B (n = 16)	124.26	139.61	0.01	-15.35
p-value	0.95	0.07		0.01

Table 6. Correlation between BMI and reduction in blood glucose level

	Change in FBS from baseline to first 2 weeks	Change in FBS from Day 14 to Day 28	Change in 2H PPBS from baseline to first 2 weeks	Change in 2H PPBS from Day 14 to Day 28
Pearson Correlation between BMI and -	-0.19	0.09	-.16	0.29
p-value	0.48	0.73	0.56	0.29

Table 7. Likert Scale for evaluation of the acceptability of apple cider vinegar among pregnant patients

	Strongly Agree (Lubos na sumasang-ayon)	Agree (Sumasang-ayon)	Neutral (Alanganin)	Disagree (Hindi sumasang-ayon)	Strongly Disagree (Lubos na hindi sumasang-ayon)
1) The Apple cider vinegar has an acceptable taste (Ang Apple Cider Vinegar ay may katanggap-tanggap na lasa)	1 (3.1%)	19 (59.4%)	10 (31.3%)	2 (6.3%)	0 (0%)
2) Bedtime ingestion of Apple cider Vinegar is tolerable (Ang pag-niom ng Apple Cider Vinegar bago matulog ay mapagtiisan)	3 (9.4%)	23 (71.9%)	5 (15.6%)	0 (0%)	0 (0%)
3) The price of Apple Cider Vinegar is affordable (Ang apple cider vinegar ay abot-kaya)	0 (0%)	12 (37.5%)	19 (59.4%)	1 (3.1%)	0 (0%)
4)The Apple Cider Vinegar causes epigastric discomfort (Ang Apple Cider Vinegar ay nag-dudulot ng pangangasim ng sikmura)	0 (0%)	1 (3.1%)	17 (53.1%)	13 (40.6%)	1 (3.1%)
5) The Apple Cider vinegar did not cause any adverse reactions to me (Ang Apple Cider Vinegar ay walang naidulot na pa salungat na reaksyon sa akin)	2 (6.3%)	18 (56.3%)	11 (34.4%)	1 (3.1%)	0 (0%)
*Specify if there are any adverse reactions (Uriin kung meron mang kahit anong pasalungat na reaksyon)	Soft stool: 1 (3.1%) None: 31 (96.9%)				

with the reduction on the blood sugar levels. Results showed a marginally significant correlation (0.09) between the degree of reduction of fasting blood sugar levels and the BMI in the subjects receiving the same amount of apple cider vinegar (Table 6). A greater reduction in the blood sugar level was noted in patients with higher BMI during the period when patients were given the ACV.

A Likert scale was used to determine the acceptability of ACV in pregnant patients. As to its taste, 59 % attested that it was tolerable. As to its ease of use, majority (72%) agreed that bedtime ingestion was easy and tolerable as well. Majority (59.4%) said that the price was affordable. Only 1 patient experienced acid reflux initially, but 53-56 % attest that they were neutral as to occurrence of acid reflux or any other adverse reactions. (Table 7)

DISCUSSION

The results of this study suggest that ACV ingestion at bedtime may favorably reduce the FBS and the 2H blood glucose in patients diagnosed with GDM. This is consistent with the study of White et al, wherein bedtime ingestion of vinegar after mealtime was employed leading to decreased morning FBS. This suggests that there could be an alternative mechanism independent of the ingestion of food.²

The antiglycemic effect of acetic acid, which is the active ingredient of ACV has been studied using human, animal, and cell culture data. These mechanisms are attributed to reduced starch digestion and/or delayed gastric motility, increased satiation leading to lower food intake, reduced hepatic gluconeogenesis and glycogenolysis but promoting hepatic and skeletal glycogen storage.^{2,4,16} Moreover, vinegar seems to be effective in suppressing the speed of entry of glucose into the blood circulation and in effect, it lowers the peak glucose and insulin secretion. In a study of Ostman, it was found out to have a slowing effect, not a reducing effect, which may be beneficial in improving insulin sensitivity in diabetics.¹⁹ Again, the slowing effect may be due to the ability of the ACV to slow gastric emptying rates.²⁰

Many of these mechanisms are in fact being harnessed by oral hypoglycemic pharmaceuticals. In this study, reductions in the FBS and the 2H blood glucose were noted with the addition of ACV to diabetic diet, however its magnitude are less than that observed in other trials examining the efficacy of pharmaceutical hypoglycemic agents. Nevertheless, ACV still presents as a good complementary adjuvant for diabetics.^{2,4}

This study has relatively a small sample size (n=32), which could possibly affect the findings leading to non-statistically significant or marginally significant results. Taking into account that the limited sample size could not be representative of the target population, the

cross over design was employed to reduce the error variance due to individual differences and to ensure that individual differences in response to control and apple cider vinegar intervention would be held constant.⁴

In a meta-analysis of the hypoglycemic effects of vinegar done by Rezai et al., several studies separately evaluated the effects of vinegar on the FBS and on post prandial glycemia, respectively. As mentioned earlier, these tests were deferred. Hence in this study, a 75g OGTT, which includes the fasting blood sugar (FBS) and the 2nd hour blood sugar (2hBS) were chosen because these tests measured different alterations, which are useful in combination.¹²

Although there is paucity of information as regards the length of time that diet should be maintained before initiation of insulin, the POGS CPG, Consensus on Diabetes Mellitus in Pregnancy, 2011, 2nd ed. recommended that if glycemic control is not achieved within 2 weeks of MNT, then insulin therapy should be started.^{3,22} Hence the 2-week period per treatment was adopted and those with a more elevated blood sugar from the baseline after the 2-week MNT were excluded in the study.

A correlation between baseline BMI and efficacy of ACV in 75g OGTT changes was also done. In this study, a marginally significant correlation between the degree of reduction of blood sugar levels and the BMI in the subjects receiving the same amount of ACV was noted. A greater reduction in the blood sugar level was noted in patients with higher BMI during the period when patients were given the ACV. Closer examination of the data revealed that these patients (n=9) with BMI >25 kg/m² had a relatively higher baseline blood sugar values compared to others. This finding is consistent with the findings of White et al, wherein vinegar treatment was particularly effective for subjects with FBS of >7.2 mmol/L as compared to those <7.2 mmol/L.² With regards to the rest of the subjects, no significant correlation was noted. This was consistent with the findings of Cai et al., where regardless of the type of the hypoglycemic agent used and patient's BMI, there was no association with its efficacy in blood sugar changes from baseline.¹⁸

The acceptability of ACV to pregnant patients as to its taste, ease of use at bedtime, occurrence of acid reflux or any other adverse reactions was remarkable. It is notable that contrary to what is expected of vinegar, the diluted ACV did not cause a significant acid reflux. This was consistent with the study of Yeh, Z. where effects of ACV in subjects with Gastroesophageal Reflux Disease (GERD) were studied. Findings showed that ingestion of diluted ACV seemed to provide some heartburn relief that it might provide a better esophageal clearance for GERD patients whose etiology is not secondary to hyposensitive esophageal mucosa to acid stimulation. The possible reason could be because the diluted vinegar had a pH of 3.0 and that the acid infusion in the upper third part of esophagus significantly increase the saliva

secretion. The saliva might have neutralized the content, and increased primary peristalsis from swallowing extra saliva might have helped to clear the esophagus as well.²²

CONCLUSION

There was a marginally significant reduction in the FBS when the ACV was administered and a clinically significant reduction in the 2nd hour blood sugar levels after 2 weeks of diabetic diet with ACV. After ACV was withdrawn, there was a statistically and clinically significant rise in the 2nd hour blood sugar indicating that ACV has a potential complementary hypoglycemic effect that could be harnessed to become an adjunct therapy for gravidas with GDM.

LIMITATIONS

The main limitation of the study was the paucity of published researches on both pregnant animal and

human subjects that are needed to establish a stronger statistical evidence on the hypoglycemic effect of ACV on gravidas. The relatively small sample size that this study was able to achieve was also a limitation. Also, a much more uniform and programmed diabetic diet tailored on their allowed caloric requirements and taken under direct supervision of the researcher was not undertaken due to lack of resources. The different dietary composition may have lipids and proteins that may have a synergistic or confounding effect on vinegar.⁴

RECOMMENDATION

Further studies to evaluate effects of dietary ACV on chronic disease outcomes including perinatal morbidity and further evaluation of long-term indicators of elevated blood glucose such as hemoglobin A1C is highly recommended. ■

REFERENCES

1. Magon, N., Sheshiah, V. Gestational Diabetes Mellitus: Non-Insulin Management. *Indian Journal of Endocrinology and Metabolism*. 2011.
2. White, A., Johnston, C. Vinegar Ingestion at Bedtime Moderates Waking Glucose Concentrations in Adults with Well-Controlled Type 2 Diabetes. 2007.
3. Philippine Obstetrical and Gynecological Society Clinical Practice Guidelines (POGS CPG) Consensus on Diabetes Mellitus in Pregnancy, 2nd ed. 2011
4. Rezai, S., Winsor, R., Giovane, R., Henderson, C. A Review of the Hypoglycemic Effects of Vinegar and its Potential Benefit in Gestational Diabetes Mellitus. *Obstetrics and Gynecology International Journal*, Volume 4. 2016
5. Budak, N., Aykin, E., Seydim, A. Functional Properties of Vinegar. *Journal of Food Science*. 2014.
6. Crowther, C., Hiller, J. Effect of treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes. *The New England Journal of Medicine*, Vol 352 No. 24. 2005.
7. Material Safety Data Sheet. Accessed: <http://avogadro.chem.iastate.edu/MSDS/aglac.htm>. 2001.
8. Sherertz, P. Virginia Department of Health, Division of Health Hazards control. 1994.
9. Cunningham, F. Gary, Leveno, Kenneth J., Bloom, Steven, L., et al. *Williams Obstetrics*, 24th Edition. McGraw-Hill Education. 2014
10. Dennis, B., Derr, J. Well-Controlled Diet Studies in Humans. A Practice Guide to Design and Management. Chapter 2 Statistical Aspects of Controlled Diet Studies. 1st Ed. American Dietetic Association. 1999.
11. Johnston, C., Gaas, C. Vinegar: Medical Uses and Antiglycemic Effect. 2006.
12. Schanca, GP., Ross, A. The Significance of Impaired Fasting Glucose Versus Impaired Glucose Tolerance. *Diabetes Care*, Volume 26, Number 5. 2003.
13. Iman, M., Moallem, SA. Effect of Apple Cider Vinegar n Blood Glucose Level in Diabetic Mice. *Pharmaceutical Sciences*. 2015. Volume 20, 163-168.
14. Lim, J., Henry, C. Vinegar as a functional ingredient to improve postprandial glycemic control—human intervention findings and molecular mechanisms. *Mol. Nutr. Food Res*. 2016. Vol 60, 1837-1849, 1837
15. Jarvis, D.C. *Folk Medicine: A New England Almanac of Natural Health Care*. International and Pan-American Copyright Conventions. 1958. ISBN 0-449-20880-X
16. Lim, J., Henry, C., Haldar, S. Vinegar as a functional ingredient to improve postprandial glycemic control—human intervention findings and molecular mechanisms. *Mol Nutr Food Res*. 2016.
17. Hlebowicz, J., Darwiche, G., Bjorgell, O. Effect of apple cider vinegar on delayed gastric emptying in patients with type 1 diabetes mellitus: a pilot study. *BMC Gastroenterology*. 2007.
18. Cai, X., Yang, W. Baseline, Gao, X. Baseline Body Mass Index and the Efficacy of Hypoglycemic treatment in Type 2 Diabetes; A Meta-analysis. 2016. PLOS ONE DOI: 10.1371/journal.pone.0166625
19. Ostman E, et al. Vinegar supplementation lowers glucose and insulin responses and increases satiety after a bread meal in healthy subjects. *Eur J Clin Nutr*. 2005.
20. Hlebowicz J, et al. Effect of apple cider vinegar on delayed gastric emptying in patients with type 1 diabetes mellitus: a pilot study. *BMC Gastroenterol*. 2007.
21. Menato, G., Bo, S., Signorile, A., et al. Current Management of Gestational Diabetes Mellitus. *Expert Rev of Obstet Gynecol*. 2008. 3(1):73-91.
22. Yeh, Z., Is Apple Cider Vinegar Effective for Reducing Heartburn Symptoms Related to Gastroesophageal Reflux Disease? 2015. Arizona State University.