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Effect of Natural Antioxidant Supplementation of Rose Cider (*Rosa damascena*) on Oxidative Stress in High-Risk Pregnant Women: An Analysis of Malondialdehyde (MDA) Biomarkers

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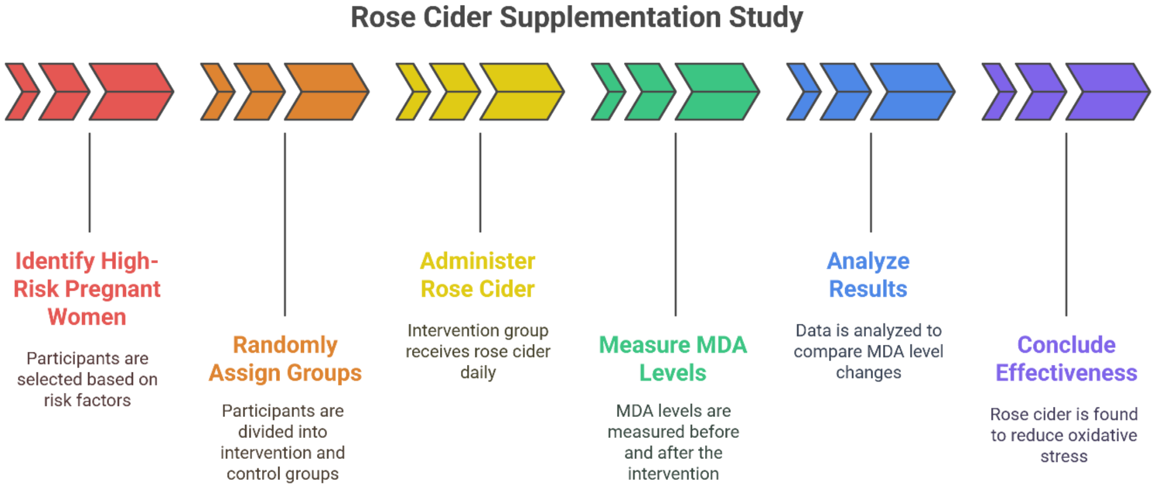
ABSTRACT

Pregnancy in high-risk mothers is often linked to increased oxidative stress, which can cause obstetric complications and impair fetal development. Malondialdehyde (MDA), a byproduct of lipid peroxidation, is a commonly used biomarker to assess oxidative stress levels. Nutritional interventions based on natural antioxidants are gaining attention as a strategy to reduce oxidative stress during pregnancy. Rose cider (Rosa damascena) contains phenolic compounds and flavonoids with antioxidant properties. This study aimed to evaluate the effect of rose cider supplementation on MDA levels in high-risk pregnant women. A quasi-experimental design with ~~a~~ pretest-posttest measurements was conducted involving 60 high-risk pregnant women randomly assigned to two groups: the intervention group received 250 ml of rose cider daily for 30 days, while the control group received a placebo. MDA levels were measured before and after the intervention using the thiobarbiturate (TBA) spectrophotometry method. Results showed a significant reduction in MDA levels in the intervention group compared to the control group ($p < 0.01$). The intervention group's MDA decreased by 1.87 ± 0.45 µmol/L, whereas the control group's reduction was only 0.42 ± 0.31 µmol/L. These findings demonstrate the effectiveness of antioxidant compounds in rose cider in lowering oxidative stress among high-risk pregnant women. This supports the potential of herbal-based supplements as preventive measures in managing high-risk pregnancies. Further research is recommended to explore the long-term effects and molecular mechanisms underlying this supplementation.

Key Messages:

- Oxidative stress is a major risk factor in high-risk pregnancies that can negatively impact the health of the mother and fetus.
- Natural antioxidant-based interventions can be a non-pharmacological preventive strategy in the management of high-risk pregnancies that are safe and effective

GRAPHICAL ABSTRACT



INTRODUCTION

Pregnancy is a physiological condition that demands complex metabolic and immunological adaptations to support the optimal growth and development of the fetus. However, in high-risk pregnancies, such as those characterized by gestational hypertension, preeclampsia, gestational diabetes, or multiple pregnancies, there is a significant increase in oxidative stress that disrupts the balance between free radical production and the body's antioxidant defense system (1, 2). Uncontrolled oxidative stress contributes to endothelial dysfunction, systemic inflammation, and perinatal complications, worsening the prognosis for both mother and fetus (3, 4).

One of the widely used biomarkers to assess oxidative stress is Malondialdehyde (MDA), a final product of lipid peroxidation indicating oxidative damage to cell membranes. Elevated MDA levels in high-risk pregnant women have been linked to increased incidences of preeclampsia, intrauterine growth restriction (IUGR), and preterm labor (5, 6). Therefore, safe and effective interventions to reduce oxidative stress accumulation are crucial in managing high-risk pregnancies.

Natural antioxidant supplementation is a nutritional strategy utilizing bioactive compounds from plants or natural sources to neutralize free radicals. Natural antioxidants such as flavonoids, polyphenols, vitamin C, and carotenoids work by scavenging reactive oxygen species (ROS), protecting cellular components from damage (7). In high-risk pregnancies, oxidative stress can cause placental dysfunction and systemic complications. Supplementation with natural antioxidants is considered safer than synthetic options and has minimal side effects, making it a promising choice for preventing oxidative stress-related complications.

Rose cider (Rosa damascena Mill.), a natural antioxidant source, contains flavonoids (kaempferol, quercetin), phenolic acids (gallic, sinapic acids), and essential oils. Pharmacological studies demonstrate that these compounds enhance endogenous antioxidant capacity, reduce lipid peroxidation, and inhibit inflammatory pathways activated by oxidative stress (8). Rose extract also increases antioxidant enzymes activity such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), which maintain cellular integrity during pregnancy. However, clinical evidence of its efficacy in pregnant populations remains limited, necessitating further research.

MDA is the most common biomarker for lipid peroxidation, reflecting oxidative damage levels in plasma or serum (9). High-risk pregnant women tend to show elevated MDA levels, indicating an imbalance between ROS and antioxidant defenses. Thus, MDA measurement is a critical indicator for evaluating antioxidant intervention effectiveness. A reduction in MDA following supplementation signals decreased oxidative stress and potential mitigation of pregnancy complications (10).

Natural antioxidant-based nutritional interventions are gaining attention as preventive

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approaches. Rose cider (Rosa damascena Mill.), rich in flavonoids, vitamin C, and phenolic compounds, exhibits high antioxidant capacity. In vitro and in vivo studies reveal that rose flower extract scavenges free radicals and significantly lowers MDA levels in animal models (11, 12). Nevertheless, scientific evidence regarding clinical effectiveness in high-risk pregnant women is still scarce.

There remains a knowledge gap concerning plant-based supplements for preventing or reducing oxidative stress during pregnancy. Previous research has mainly focused on synthetic supplements or conventional vitamins, while phytotherapy with objective biomarkers like MDA in high-risk pregnancies is rare. Additionally, molecular mechanisms underlying the protective effects of natural supplements in gestation are not fully understood.

This study aims to investigate the effect of rose cider supplementation on oxidative stress biomarkers, particularly MDA, in high-risk pregnant women. Using experimental design and biochemical analysis, this research is expected to contribute to developing safe, natural antioxidant-based supportive therapies for managing high-risk pregnancies. The findings may also facilitate integrating modern medicine and plant-based therapies to improve maternal health care quality.

METHODS

Research Design

This study used a quasi-experimental design with a pretest-posttest control group design approach to evaluate the effect of natural antioxidant supplementation from rose cider on the levels of oxidative stress biomarker Malondialdehyde (MDA) in high-risk pregnant women. This design was chosen to allow comparisons between intervention and control groups before and after treatment, while observing changes in biomarkers as objective biological indicators (13, 14).

Population and Sample

The target population consisted of pregnant women in their second to third trimester, identified as high-risk due to conditions such as a history of preeclampsia, gestational hypertension, or gestational diabetes. Participants were recruited from Maternal and Child Clinics and referral health centers in urban areas using purposive sampling based on inclusion criteria: gestational age between 20 and 34 weeks, not currently taking other antioxidant supplements, and willingness to comply with all study procedures. Exclusion criteria included severe medical conditions potentially affecting oxidative status (e.g., active infections or autoimmune diseases). A total of 60 respondents were enrolled, with 30 participants each in the intervention and control groups, determined by power analysis ($\alpha = 0.05$, power = 80%). The mean age and BMI of participants were recorded as part of population characteristics.

Materials and Instruments

The rose cider used is sourced from GMP (Good Manufacturing Practice) certified local herbal producers and has gone through phytochemical content tests to ensure the concentration of flavonoids and active phenolics. Each participant in the intervention group was given 250 mL of rose cider once a day for 4 weeks. The control group received no additional treatment other than routine antenatal care. MDA levels were measured by taking 5 mL of venous blood before and after the intervention. MDA analysis used the Thiobarbituric Acid Reactive Substances (TBARS) method and was carried out in an accredited laboratory using a UV-Vis spectrophotometer (Shimadzu UV-1800, Japan).

Data Collection Procedure

Before intervention, all participants were given a detailed explanation of the objectives, procedures, potential benefits, and risks of the research before signing the informed consent form. The confidentiality of participants' identities and data is strictly maintained in accordance with bioethical principles. Participants underwent an initial laboratory examination to measure MDA levels as a baseline value. During the intervention period, the adherence to rose cider consumption was monitored through daily records and weekly visits. After 4 weeks, a second blood sample is taken and analyzed for changes in MDA levels. Demographic data and clinical characteristics were also collected through structured interviews and medical records (15).

Data Analysis

The data obtained was analyzed using IBM SPSS software version 26.0. The normality test was

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performed using the Kolmogorov-Smirnov (16). Comparison of changes in MDA levels in the group (pretest-posttest) was analyzed using a paired t-test or Wilcoxon signed-rank test when the data were abnormal. Differences between groups compared to independent t-test or Mann-Whitney U test. The significance level was set at $p < 0.05$.

Ethical Considerations

This research has received approval from the Health Research Ethics Committee of Poltekkes Kemenkes Riau Pekanbaru (Approval Number: 078/KEPK-PKR/IV/2024).

RESULTS

This study involved 60 high-risk pregnant women who were randomly divided into two groups, namely the intervention group (n=30) and the control group (n=30). The intervention group received rose cider supplementation for 4 weeks, while the control group was not given any treatment. Before the intervention, the two groups showed no significant differences in basic characteristics, such as age, gestational age, body mass index (BMI), and history of comorbidities ($p > 0.05$). This shows that both groups have homogeneous characteristics, which strengthens the validity of the research results by ensuring that other factors that can affect the research variables have been well controlled.

Malondialdehyde (MDA) Measurements Before and After Intervention

Prior to the intervention, the average MDA level in the intervention group was 5.83 ± 1.22 nmol/mL, while in the control group it was 5.79 ± 1.30 nmol/mL. This difference was not statistically significant ($p = 0.87$), suggesting that both groups had similar levels of oxidative stress at the start of the study. After 4 weeks of rose cider supplementation, a significant decrease in MDA levels was found in the intervention group. The average MDA level of the intervention group decreased to 3.46 ± 0.95 nmol/mL ($p < 0.001$). On the other hand, the control group showed a non-significant decrease in MDA levels, from 5.79 ± 1.30 nmol/mL to 5.62 ± 1.28 nmol/mL ($p = 0.21$) (Figure 1).

Table 1. Comparison of MDA Levels Before and After Intervention

Group	Measurement Time	MDA (nmol/mL) Mean ± SD	Average Change	P-value in a group
Intervention (n=30)	Before	5.83 ± 1.22	↓ 2.37	p < 0.001
	After	3.46 ± 0.95		
Control (n=30)	Before	5.79 ± 1.30	↓ 0.17	p = 0.21
	After	5.62 ± 1.28		

Posttest Comparison Between Groups

Comparison of Malondialdehyde (MDA) levels between the intervention group and the control group after the intervention showed a statistically significant difference ($p < 0.001$) (Table 2). The intervention group showed a much greater reduction in MDA levels compared to the control group, indicating that rose cider supplementation had a significant impact on reducing oxidative stress levels, interactions with other medical interventions during pregnancy. The potential of rose cider in improving maternal and fetal health can be utilized optimally in clinical practice.

Table 2. Comparison of MDA Levels Between Groups

Measurement Time	Intervention MDA Rate (Mean ± SD)	Control Up MDA (Mean ± SD)	P values Between Groups
Before	5.83 ± 1.22	5.79 ± 1.30	p = 0.87
After	3.46 ± 0.95	5.62 ± 1.28	p < 0.001

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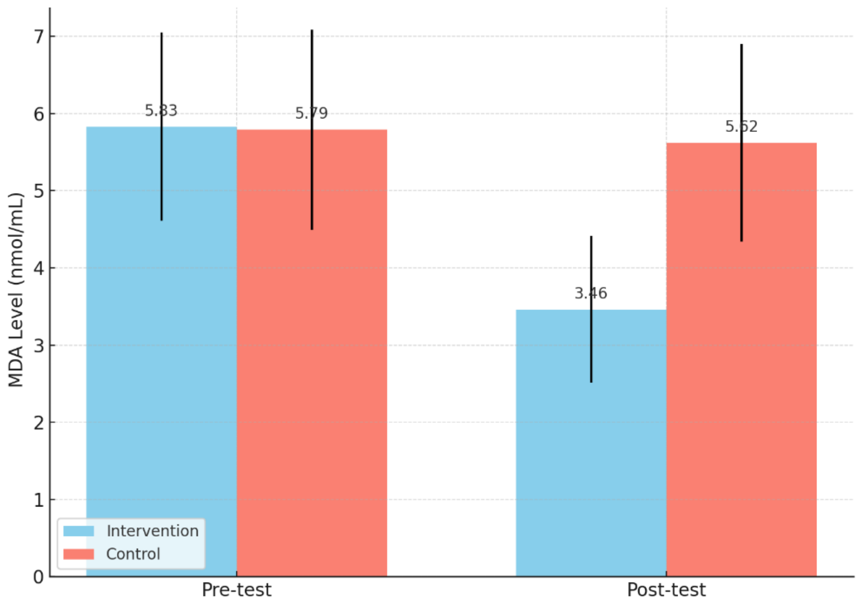

Figure 1. Comparison of MDA Levels Before and After Intervention

DISCUSSION

The results of this study show that natural antioxidant supplementation in the form of rose cider significantly lowers Malondialdehyde (MDA) levels in high-risk pregnant women. MDA is the end product of the lipid peroxidation process which is often used as a biomarker of oxidative stress. Increased levels of MDA reflect oxidative damage that occurs due to an imbalance between free radical production and the ability of the body's antioxidant system to neutralize it. Therefore, the decrease in MDA levels after the intervention reflects an increase in the body's antioxidant defense capacity, which is crucial in maintaining pregnancy health, especially in high-risk populations such as people with preeclampsia, gestational hypertension, or gestational diabetes mellitus (19, 20).

The effectiveness of rose cider in lowering MDA levels can be attributed to the content of bioactive compounds in it, such as flavonoids (quercetin, kaempferol), polyphenols, and vitamin C. These compounds are known to have strong antioxidant activity through various mechanisms, including free radical capture, inhibition of oxidative reaction chains, and stimulation of endogenous antioxidant systems. Several previous studies have supported these results, as reported by Hapsari et al. and Gupta et al., which show that rose extract has antioxidant capacity equivalent to even surpassing synthetic antioxidants in the face of chronic oxidative conditions (21, 22).

The significant decrease in MDA in the intervention group and the insignificance of the change in the control group reinforce the hypothesis that these effects directly result from the intervention given. This underscores the potential of rose cider as an antioxidant agent that is not only effective but also safe to use during pregnancy. Another advantage of using natural antioxidants such as rose cider is their high safety profile, especially when compared to synthetic antioxidants which in some cases can have toxic effects if used long-term or at high doses. In the context of pregnancy, where fetal safety is a major concern, such herbal non-pharmacological preventive approaches are highly relevant and have great potential to be integrated into integrated antenatal care protocols, particularly in areas with a high prevalence of high-risk pregnant women and limited access to specialist health services.

Although the results of this study are promising, there are several limitations that need to be considered. First, the duration of the intervention lasting only 4 weeks may not be enough to capture the long-term impact of rose cider use on maternal and fetal health. Second, the main focus of this study was on only one biomarker of oxidative stress, MDA, without evaluating other parameters of the endogenous antioxidant system such as the activity of the enzyme superoxide dismutase (SOD), glutatiate peroxidase (GPx), or catalase. In fact, to get a more comprehensive picture of the oxidative status of the body, it is necessary to take measurements of these various biomarkers. Third, although homogeneity between

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groups had been confirmed at the beginning of the study, the potential influence of other factors such as diet, physical activity, and psychological stress levels had not been completely eliminated.

Going forward, it is recommended to conduct further research with a longitudinal design and involving a larger sample size to increase the external validity of the findings. In addition, exploration of optimal doses, ideal duration of supplementation, and interactions with other interventions during pregnancy (such as iron or folic acid supplementation) are important to ensure the effectiveness and safety of the broader use of rose cider. Translational research that bridges the gap between laboratory test results and clinical practice is also needed to ensure that these interventions can be implemented practically and efficiently in maternal health care systems. Overall, this study makes an important contribution in the field of maternal health by highlighting the potential of rose cider as a safe, effective, and sustainable natural antioxidant supplement in supporting a healthy pregnancy, especially in the pregnant population with high risk of oxidative stress.

The presence of bioactive compounds such as flavonoids, phenolic acids, and essential oils in rose cider has been confirmed through phytochemical analysis using methods like high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), and spectrophotometric assays. These methods allow for accurate identification and quantification of antioxidant compounds. Furthermore, numerous published scientific studies consistently report the presence of these compounds in rose extracts and cider, supporting the claims of the natural antioxidant activity of this material. Rose extract is known to contain a variety of bioactive compounds that play an important role in antioxidant mechanisms, including flavonoids, phenolic acids, anthocyanins, and tannins. Flavonoids such as quercetin and kaempferol are the main components that have been widely researched to have a high ability to neutralize free radicals through the mechanism of electron or hydrogen delivery to reactive molecules. Phenolic acids, such as gallic acid and ellagic acid, also contribute to cellular protection by inhibiting lipid peroxidation processes and improving the balance of the redox system in the body. The presence of these compounds makes rose cider a potential natural source of antioxidants to treat conditions associated with oxidative stress (21). In this study, the rose cider used underwent phytochemical content testing at an accredited laboratory to verify the presence and concentration of active compounds, ensuring the quality and efficacy of the supplement provided to the participants.

In pregnancy, especially in high-risk pregnant women, there is an increase in metabolic activity, oxygen demand, as well as significant hormonal changes, which can collectively increase the production of reactive oxygen species (ROS). If left unchecked, ROS can cause damage to biomolecular structures such as lipids, proteins, and DNA, which can further trigger obstetric complications such as preeclampsia, gestational hypertension, gestational diabetes mellitus, and fetal growth disorders. Therefore, preventive strategies that are able to reduce the impact of oxidative stress are very crucial in efforts to improve the quality of pregnancy (22).

The findings in this study provide evidence that 4 weeks of rose cider supplementation significantly lowered levels of Malondialdehyde (MDA), a biomarker widely used to assess lipid peroxidation levels and oxidative damage. The decrease in MDA levels in the intervention group, which is statistically significant, suggests that the active compounds in rose cider work effectively in stabilizing ROS and strengthening the body's endogenous antioxidant defenses. The fact that the control group did not experience significant reductions further supports the claim that the decrease in oxidative stress in the intervention group was not the result of natural or external factors, but rather a direct result of the administration of rose pollen.

Rose cider has great potential to be developed as a safe and natural non-pharmacological intervention in the management of high-risk pregnancies. Its use is also considered relatively safe because it comes from herbal ingredients that have been used for a long time in traditional medicine and cosmetics, and generally have minimal side effects. However, while the results of this study are promising, it is important to note that the long-term effectiveness and safety of rose cider still need to be validated through further studies.

Further research is recommended to explore the molecular mechanisms underlying the antioxidant effects of rose cider, including its effect on the expression of antioxidant genes, redox enzymes

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such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase. In addition, clinical studies with larger populations, randomized controlled trial (RCT) designs, and longer monitoring periods are needed to identify optimal doses, frequency of administration, and long-term safety of consumption, for both mother and fetus. The integration of these scientific findings into evidence-based obstetric practice guidelines can also strengthen preventive and promotive approaches in pregnant women's health services.

Research Limitations and Suggestions for Further Research

Despite promising findings, this study has limitations. The 4-week intervention period may not capture long-term effects on maternal and fetal outcomes. Only MDA was measured as an oxidative stress biomarker, while additional parameters such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase activities should be evaluated in future studies for a comprehensive assessment. Potential confounding factors like diet, physical activity, and psychological stress were not fully controlled. Future research should involve larger sample sizes, longer follow-up periods, and randomized controlled trial designs to confirm these findings. Investigations into optimal dosing, timing, and interactions with other pregnancy-related supplements (e.g., iron, folic acid) are warranted. Translational studies bridging laboratory findings to clinical practice will enhance implementation in maternal health care.

CONCLUSION

The results of this study showed that rose cider supplementation significantly lowered Malondialdehyde (MDA) levels, a major biomarker of oxidative stress, in high-risk pregnant women. This effect is thought to be strong from the content of flavonoids, polyphenols, and vitamin C in rose cider which act as natural antioxidants, are able to neutralize free radicals, and inhibit lipid peroxidation.

These findings provide a scientific basis that rose cider has the potential to be developed as a safe and effective non-pharmacological intervention to reduce oxidative stress during pregnancy, particularly in high-risk pregnant women. However, to support widespread clinical application, further research with a long-term design is needed, involving other endogenous antioxidant biomarkers, and considering optimal dosage and long-term safety for both mother and fetus.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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