

## **Probiotic for Pregnancy: A Review**

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**Abstract.** Mother Mortality Rate (MMR) is a health indicator status in a country. We need a strategy to increase the health of pregnancy. Probiotic is a new pharmacotherapy for healthy. Recent studies show that probiotic is safe for pregnancy. This paper aims to describe the benefits of probiotic for pregnancy. This systematic review was based on the search of Google Scholar, Pubmed, Ebsco, Cochrane, Science Direct and DOAJ published from 2010 to 2019. There were 285 articles published last ten years related to probiotic for pregnancy. 95 articles were excluded because they had same titles. 33 articles were not relevant. After using inclusive and exclusive criteria, there were 11 eligible articles. The research showed probiotics had many benefit and increased pregnancy health. Probiotics could reduce blood, stress oxidative, and risk diabetes gestational. It was concluded probiotics could increase the healthy status of pregnancy.

### **1. Introduction**

Maternal morbidity and mortality are health indicators of a county. The high maternal morbidity and mortality rates indicate poor quality of health service. Data from World Health Organization (WHO) in 2017 shows that MMR in the world was at 216 per 100.000 live births [1]. Research stated that from 2003 to 2009 in 115 countries, the most common causes of maternal death were bleeding, hypertension and sepsis. In addition, maternal morbidity can also cause another factor, such as anemia, gestational diabetes mellitus, and others.[2].

When it is not handled properly, it can affect the health of the fetus. Therefore, there is a need of maternal health. Complementary therapy can be one effort to improve the health status of the mother during pregnancy. Various therapies have been implemented such as antenatal yoga, remembrance therapy, relaxation, aromatherapy, and others.

Today, the use of probiotics during pregnancy has been developed. The use of probiotic is safe and beneficial for pregnancy. This review discusses the benefits of probiotics for pregnant women.

### **2. Research Method**

This review used articles from Google Scholar, Science Direct, Pubmed, DOAJ, Cochrane, and Ebsco published from 2010 to 2019. The inclusive criteria used in writing this article were full text articles, concerning with woman pregnancy, using English language, and discussing the benefits of probiotics in pregnancy. The exclusive criteria in this article was - non-English language articles. The keywords were probiotics, pregnancy, blood pressure, preeclampsia, oxidative stress, and gestational diabetes.

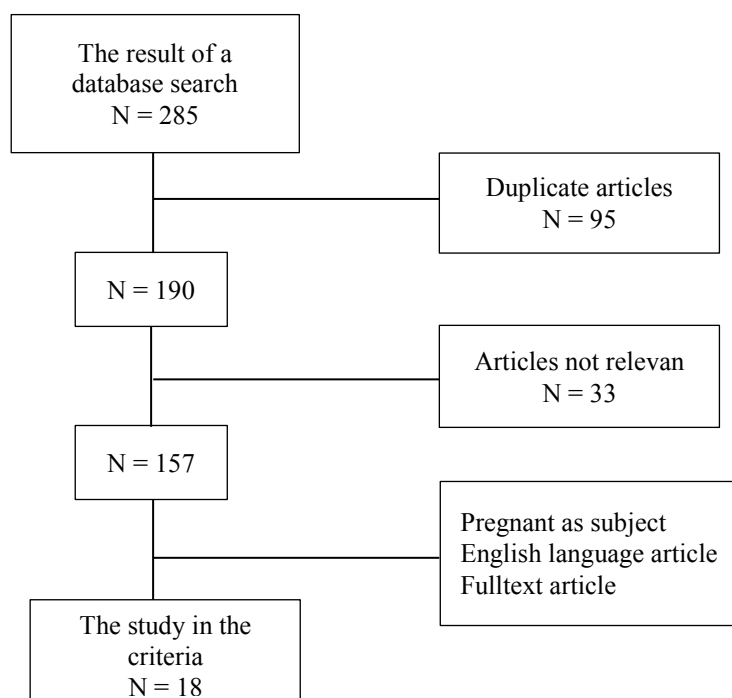


Figure 1. Flowchart of the exclusion process and final selection

### 3. Result and Discussion

#### 3.1. Definition of probiotic

World Health Organization and Food Agriculture Organization defines probiotics as living microorganisms. When it is given sufficient quantities, it can benefit their hosts. According to this definition, the intended number was around  $10^6$ - $10^8$ . [3]

Some ideal criteria for probiotic strains are that they provide benefits to their hosts, non-toxic; they contain a large number of living cells and are able to survive well in some environmental conditions and metabolized in the intestine, remain alive during storage and at the time used. Some of the popular probiotic used microorganisms are *lactobacillus rhamnosus*, *lactobacillus reuteri*, *bifidobacteria* and certain strains of *lactobacillus casei*, and *lactobacillus achidphilus* group. Probiotic products can contain a single strain or a mixture of two or more strains. [3-5].

#### 3.2 The safe status of probiotic during pregnancy

Several studies have shown that the use of probiotics is safe during pregnancy. A meta-analysis study was conducted on 1500 pregnant women. Most of the subjects were in 32 to 36 weeks of pregnancy. There was one study in first trimester. The results showed no difference in the risk of cesarean birth, birth weight, and gestational age in the group given probiotic *lactobacillus sp* along, or combination with *bifidobacterium* and the placebo group [6]. In other studies, probiotics during pregnancy were considered safe and did not cause health effects. The use of probiotics during pregnancy could provide health benefits for pregnant women [7].

#### 3.3 Benefit of probiotic in pregnancy

##### 3.3.1 Reduce blood pressure and risk of preeclampsia

Preeclampsia is a condition where the blood pressure of the mother is more than normal (140/90 mmHg), entailed by urine protein. This situation can develop into severe preeclampsia and eclampsia

so that it can increase the risk of death in mother and baby. Preeclampsia begins with an increase in blood pressure during pregnancy [8].

**Table 1.** Probiotic on blood pressure

Author	Subject	Content	Dose (CFU)	Duration	Source	Outcome
Majid, et al 2017[9]	Pregnant diagnosed gestational diabetes mellitus	<i>Lactobacillus acidophilus LA-5</i>	>4x10 <sup>9</sup>	6 weeks	capsule	Reduce SBP p 0,008
		<i>Bifidobacterium BB-12</i>				Reduce DBP P <0,001
		<i>Streptococcus thermophilus STY-31</i>		8 weeks		Reduce SBP p 0,002
		<i>Lactobacillus delbrueckii bulgarius</i> <i>LBY-27</i>				Reduce DBP P <0,001

Research by Majid showed that consumption of probiotics could reduce systolic and diastolic blood pressure in pregnant women with diabetes mellitus. It used combination probiotics. After 6 weeks intervention, it significantly reduced systolic blood pressure (p 0,008) dan diastolic blood pressure (p<0,001) [9]. Primiparous pregnant women who consumed probiotic milk (*lactobacilli* 10<sup>8</sup>) at least 140 cc/day routinely every week. It could reduce the risk of all preeclampsia. In this study, among the 33.399 nulliparous women, 1.755 (5,3%) developed preeclampsia. The lower risk for preeclampsia was observed for daily probiotic intake [10]. In other study, probiotic intake in late pregnancy could reduce the risk of preeclampsia while giving milk probiotic at the early of pregnancy could reduce the risk of preterm delivery [11].

In a meta-analysis study, from 14 studies showed that probiotics could reduce systolic and diastolic blood pressure. Cellular elements or peptides derived from fermentation could inhibit the ACE enzyme that played a role in the process of angiotensin I to angiotensin II. The existence of this activity could reduce blood pressure. Some probiotics that could act as ACE inhibitors such as *Lactobacillus* strains (*L. Reuteri*, *L. Bulgarius*, *L. Rhamnosus*, and *L. Helveticu*). In addition, probiotics could prevent local and systemic inflammation so they could prevent preeclampsia [4-5].

### 3.3.2. Prevent oksidative stress

Oxidative stress is a state of imbalance between oxidants and antioxidants in the body. When the presence of free radicals (oxidants) is higher, the body needs antioxidants to balance. A state of ongoing oxidative stress could increase the risk of damage to organs in the body. Stress oxidative could cause disfunction of endotel, hypoxia, and ischemia plasenta. Several studies have shown that probiotics could act as antioxidants in the body [13].

It could be concluded that probiotics have effects in preventing oxidative and can increase antioxidants in the body, during more than 6 weeks. Probiotics have potency as antioxidants which could reduce oxidative stress and free radicals. The metabolic activity of probiotic bacteria could remove oxidants and prevent entry into the intestine [14].

In table 2, probiotic could reduce oxidative stress for 6 week intervention (3 articles), and 1 article found during 9 weeks intervention. There were 2 article showing probiotic had significances on biomarker fasting plasma glucose (FPG) and high sensitivity C reactive protein (hs-CRP) in the same duration of intervention (6 weeks). The influential effect on FGP in the article was using combination of *Lactobacillus acidophilus*, *bifidobacterium bifidum*, *lactobacillus reuteri* and *lactobacillus fermentum* ( $\beta$  -8,60 mg/dL, p<0,001). The influential effect on biomarker Hs-CRP in the article used *Lactobacillus achidophilus*, *lactobacillus casei*, and *bifidobacterium* (-2,2±2,7  $\mu$ g/mL, p<0,001).

**Table 2. Probiotic on stress oxidative**

Author	Subject	Content	Dose (CFU)	Duration	Source	Outcome
Bitar, et al 2017[15]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus</i> <i>Lactobacillus casei</i> <i>Bifidobacterium</i>	$2 \times 10^9$	6 weeks	capsule	FGP (-5,3±6,7 mg/dL, p 0,01) Hs-CRP (-2,2±2,7 µg/mL, p<0,001) MDA (-0,1±0,8, p 0,03) TAC ratio (-0,0003±0,0008, p 0,004) TAC (+65±103,3, p 0,002)
Zatullah, et al 2011[16]	Third trimester pregnant woman	<i>Streptococcus thermophilus</i> <i>Lactobacillus bulgarius</i> <i>Lactobacillus acidophilus</i> <i>Bifidobacteria</i>	$1 \times 10^7$	9 weeks	yogurt	Plasma glutathione (967,9 µmol/L, p 0,01) Erythrocyte glutathione peroxidase (163 mmol/min/ml, p 0,04) Serum 8-oxo-7,8-dihydroguanine levels (-74,3 ng/ml, p 0,04) MDA (p<0,001) Nitrit oxide (p 0,01) TAC (p 0,01)
Babadi, et al 2018[17]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus</i> <i>Bifidobacterium bifidum</i> <i>Lactobacillus casei</i> <i>Lactobacillus fermentum</i>	$2 \times 10^9$	6 weeks	capsule	MDA (p<0,001) Nitrit oxide (p 0,01) TAC (p 0,01)
Mehri 2018[18]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus</i> <i>Bifidobacterium bifidum</i> <i>Lactobacillus reuteri</i> <i>Lactobacillus fermentum</i>	$8 \times 10^9$	6 weeks	capsule	Probiotic significant reduction in: FPG (β -8,60 mg/dL, p<0,001) Hs-CRP (β -1,36 mh/L, p<0,001) MDA(β -0,50 mmol/L, p0,005)

There were 3 articles showing correlation between probiotic and malondialdehyde (MDA). The intervention for 6 weeks. The higher result of reducing level of MDA was shown by combination of *lactobacillus acidophilus*, *bifidobacterium bifidum*, *lactobacillus reuteri*, and *lactobacillus fermentum* with dose  $8 \times 10^9$ . It showed the dose could influence level MDA. Probiotic also significantly reduced total antioxidant capacity (2 articles), nitrit oxide (1 article), and serum 8-oxo-7,8-dihydroguanine levels (1 article). Probiotic could increase the plasma glutathione (1 article), erythrocyte glutathione peroxidase (1 article). The studies showed probiotic could increase antioxidant and decrease oxidant in the pregnant women.

### 3.3.3. Reducing risk on gestational diabetes mellitus (GDM)

Gestational diabetes mellitus is a condition in which a hormone made by plasenta prevents body from using insulin effectively. Several studies have reported the benefits of probiotics to reduce the risk of developing gestational diabetes. The use of probiotics started in the first trimester of pregnancy could reduce the prevalence of gestational diabetes [19].

There were 6 articles about probiotic on risk of GDM, with pregnant diagnosed gestational diabetes subjects (5 articles) and overweight and obese pregnant women (1 article). 5 articles showed effect of probiotic on reducing fasting plasma glucose (FPG). There were 4 articles showing

significant effect, and 2 articles showing no significant effect. The duration of the intervention was between 4-8 weeks. It could be caused by kinds of bacteria, and other factors.

**Tabel 3.** Probiotic on risk of diabetes mellitus

Author	Subject	Content	Dose (CFU)	Duration	Source	Outcome
Jafarnejad 2016[20]	Pregnant diagnosed gestational diabetes	<i>Streptococcus thermophilus</i> <i>Bifidobacterium breve</i> <i>Bifidobacterium longum</i> <i>Bifidobacterium invasis</i> <i>Lactobacillus acidophilus</i> <i>Lactobacillus plantarum</i> <i>Lactobacillus paracasei</i> <i>Lactobacillus delbrueckii subs bulgarius</i>	112,5x10 <sup>9</sup>	8 weeks	capsule	FPG (-2,3 mg/dL, p 0,42) Insulin (-2,5 µIU/mL, p 0,04)
Babadi, et al 2018[17]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus</i> <i>Bifidobacterium bifidum</i> <i>Lactobacillus casei</i> <i>Lactobacillus fermentum</i>	2x10 <sup>9</sup>	6 weeks	capsule	FPG (β -3,43 mg/dL, p 0,02) Insulin (β -2,29 µIU/mL, p 0,001)
Dolatkah 2015[21]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus LA-5</i> <i>Bifidobacterium BB-12</i> <i>Streptococcus thermophilus LBY-27</i>	4x10 <sup>9</sup>	8 weeks	capsule	Fasting blood sugar (-14,66 mg/dl, p 0,02) Insulin (0,09)
Karamali 2016[22]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus acidophilus</i> <i>Lactobacillus cassoisi</i> <i>Bifidobacterium</i>	2x10 <sup>9</sup> 2x10 <sup>9</sup> 2x10 <sup>9</sup>	6 weeks	capsule	FPG (-9,2±9,2 mg/dl, p < 0,001) Insulin (0,8±3,1 µIU/mL, p 0,01)
Lindsay 2015[23]	Pregnant diagnosed gestational diabetes	<i>Lactobacillus salivarius UCCI 18</i>	2x10 <sup>9</sup>	4 weeks	capsule	FPG (-4,64±0,49 mg/dl, p 0,373)
Asgharian 2018[24]	Overweight and obese pregnant woman	<i>Lactobacillus acidophilus LA-5</i> <i>Bifidobacterium lactis BB-12</i>	5x10 <sup>8</sup>	4 weeks	yogurt	FPG (-4,0, p 0,008)

Probiotic could decrease insulin serum (4 articles). 3 articles showed significant effect of probiotic and insulin serum in GDM, with the duration in 6-8 weeks. Probiotic could decrease fasting blood sugar (1 article) with duration in 8 weeks. The studies showed probiotic having benefit effect to decrease diabetes mellitus of pregnancy.

Pregnant women diagnosed gestational diabetes mellitus (GDM) were at risk and could have negative effects on mental health, including quality of life and stress. Research conducted for 56 gestational diabetes pregnant women who were given probiotic supplements (lactobacillus achidphillus, bifidobacterium, streptococcus thermophilus and lactobacillus bulgarius) for 8 weeks significantly improved quality of life ( $p = 0.045$ ) and decreased depression ( $0.042$ ). Probiotics could reduce inflammatory conditions so that it could improve quality of life. Probiotics could provide a balance of bacteria in the body so that it could block the production of the hormone serotonin and reduce symptoms of depression.[19]

#### 4. Conclusion

Probiotics were safe and provided benefits for the health of pregnant women. Mothers who consumed probiotics during pregnancy could reduce blood pressure and the risk of preeclampsia. Probiotics could prevent oxidative stress, because they could act as antioxidants. In addition, probiotics could affect insulin so that it could reduce the risk of gestational diabetes. The use of probiotics in pregnancy could be recommended as a complementary therapy in health care.

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